PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

C12Q 1/68

(11) International Publication Number:

WO 98/20157

A3

(43) International Publication Date:

14 May 1998 (14.05.98)

(21) International Application Number:

PCT/CA97/00829

(22) International Filing Date:

4 November 1997 (04.11.97)

(30) Priority Data:

08/743,637

4 November 1996 (04.11.96)

US

(71) Applicant (for all designated States except US): INFECTIO DIAGNOSTIC (I.D.I.) INC. [CA/CA]; 4ème étage, 2050, boulevard René Lévesque Ouest, Sainte-Foy, Québec G1V 2K8 (CA).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): BERGERON, Michel, G. [CA/CA]; 2069, rue Brûlard, Sillery, Québec G1T 1G2 (CA). PICARD, François, J. [CA/CA]; 1245, rue de la Sapinière, Cap-Rouge, Québec G1Y 1A1 (CA). OUELLETTE, Marc [CA/CA]; 1035 de Ploermel, Sillery, Québec G1S 3S1 (CA). ROY, Paul, H. [US/US]; 28, rue Charles Garnier, Loretteville, Québec G2A 2X8 (CA).
- (74) Agents: DUBUC, Jean, H. et al.; Goudreau Gage Dubuc & Martineau Walker, The Stock Exchange Tower, Suite 3400, 800 Place Victoria, P.O. Box 242, Montreal, Québec H4Z 1E9 (CA).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:

13 August 1998 (13.08.98)

(54) Title: SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED AN-TIBIOTIC RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN MICROBIOLOGY LABORATO-

(57) Abstract

DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample DNA from (i) any bacterium, (ii) the species Streptococcus agalactiae, Staphylococcus saprophyticus, Enterococcus faecium, Neisseria meningitidis, Listeria monocytogenes and Candida albicans, and (iii) any species of the genera Streptococcus, Staphylococcus, Enterococcus, Neisseria and Candida are disclosed. DNA-based methods employing amplification primers or probes for detecting, identifying, and quantifying in a test sample antibiotic resistance genes selected from the group consisting of blatem, blash, blash, blash, blash, blaz, aadB, aacCl, aacCl aacC3, aacA4, aac6'-IIa, ermA, ermB, ermC, mecA, vanA, vanB, vanC, satA, aac(6'-aph(2''), aad(6'), vat, vga, msrA, sul and int are also disclosed. The above microbial species, genera and resistance genes are all clinically relevant and commonly encountered in a variety of clinical specimens. These DNA-based assays are rapid, accurate and can be used in clinical microbiology laboratories for routine diagnosis. These novel diagnostic tools should be useful to improve the speed and accuracy of diagnosis of microbial infections, thereby allowing more effective treatments. Diagnostic kits for (i) the universal detection and quantification of bacteria, and/or (ii) the detection, identification and quantification of the above-mentioned bacterial and fungal species and/or genera, and/or (iii) the detection, identification and quantification of the above-mentioned antibiotic resistance genes are also claimed.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
вј	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Сопдо	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

TITLE OF THE INVENTION

5

10

15

20

25

30

35

SPECIES-SPECIFIC, GENUS-SPECIFIC AND UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTIBIOTIC RESISTANCE GENES FROM CLINICAL SPECIMENS FOR DIAGNOSIS IN MICROBIOLOGY LABORATORIES

BACKGROUND OF THE INVENTION

Classical methods for the identification and susceptibility testing of bacteria

Bacteria are classically identified by their ability to utilize different substrates as a source of carbon and nitrogen through the use of biochemical tests such as the API20E™ system (bioMérieux). For susceptibility testing, clinical microbiology laboratories use methods including disk diffusion, agar dilution and broth microdilution. Although identifications based on biochemical tests and antibacterial susceptibility tests are cost-effective, at least two days are required to obtain preliminary results due to the necessity of two successive overnight incubations to identify the bacteria from clinical specimens as well as to determine their susceptibility to antimicrobial agents. There are some commercially available automated systems (i.e. the MicroScan system from Dade Diagnostics Corp. and the Vitek system from bioMérieux) which use sophisticated and expensive apparatus for faster microbial identification and susceptibility testing (Stager and Davis, 1992, Clin. Microbiol. Rev. 5:302-327). These systems require shorter incubation periods, thereby allowing most bacterial identifications and susceptibility testing to be performed in less than 6 hours. Nevertheless, these faster systems always require the primary isolation of the bacteria as a pure culture, a process which takes at least 18 hours for a pure culture or 2 days for a mixed culture. The fastest identification system, the autoSCAN-Walk-Away™ system (Dade Diagnostics Corp.) identifies both gram-negative and gram-positive bacterial species from standardized inoculum in as little as 2 hours and gives susceptibility patterns to most antibiotics in 5.5 hours. However, this system has a particularly high percentage (i.e. 3.3 to 40.5%) of non-conclusive identifications with bacterial species other than Enterobacteriaceae (Croizé J., 1995, Lett. Infectiol. 1992, J. Clin. Microbiol. **30**:2903-2910). **10**:109-113; York *et al.*, Enterobacteriaceae, the percentage of non-conclusive identifications was 2.7 to 11.4%.

A wide variety of bacteria and fungi are routinely isolated and identified from clinical specimens in microbiology laboratories. Tables 1 and 2 give the incidence for the most commonly isolated bacterial and fungal pathogens from various types of clinical specimens. These pathogens are the most frequently associated with nosocomial and community-acquired human infections and are therefore considered the most clinically important.

10

15

20

25

30

35

Clinical specimens tested in clinical microbiology laboratories

Most clinical specimens received in clinical microbiology laboratories are urine and blood samples. At the microbiology laboratory of the Centre Hospitalier de l'Université Laval (CHUL), urine and blood account for approximately 55% and 30% of the specimens received, respectively (Table 3). The remaining 15% of clinical specimens comprise various biological fluids including sputum, pus, cerebrospinal fluid, synovial fluid, and others (Table 3). Infections of the urinary tract, the respiratory tract and the bloodstream are usually of bacterial etiology and require antimicrobial therapy. In fact, all clinical samples received in the clinical microbiology laboratory are tested routinely for the identification of bacteria and susceptibility testing.

Conventional pathogen identification from clinical specimens

Urine specimens

The search for pathogens in urine specimens is so preponderant in the routine microbiology laboratory that a myriad of tests have been developed. However, the gold standard remains the classical semi-quantitative plate culture method in which 1 µL of urine is streaked on plates and incubated for 18-24 hours. Colonies are then counted to determine the total number of colony forming units (CFU) per liter of urine. A bacterial urinary tract infection (UTI) is normally associated with a bacterial count of 10⁷ CFU/L or more in urine. However, infections with less than 10⁷ CFU/L in urine are possible, particularly in patients with a high incidence of diseases or those catheterized (Stark and Maki, 1984, N. Engl. J. Med. 311:560-564). Importantly, approximately 80% of urine specimens tested in clinical microbiology laboratories are considered negative (i.e. bacterial count of less than 10⁷ CFU/L; Table 3). Urine specimens found positive by culture are further characterized using standard biochemical tests to identify the bacterial pathogen and are also tested for susceptibility to antibiotics. The biochemical and susceptibility testing normally require 18-24 hours of incubation.

Accurate and rapid urine screening methods for bacterial pathogens would allow a faster identification of negative specimens and a more efficient treatment and care management of patients. Several rapid identification methods (Uriscreen™, UTIscreen™, Flash Track™ DNA probes and others) have been compared to slower standard biochemical methods, which are based on culture of the bacterial pathogens. Although much faster, these rapid tests showed low sensitivities and poor specificities as well as a high number of false negative and false positive results (Koening *et al.*, 1992, J. Clin. Microbiol. **30**:342-345; Pezzlo *et al.*, 1992, J. Clin. Microbiol. **30**:640-684).

Blood specimens

The blood specimens received in the microbiology laboratory are always submitted for culture. Blood culture systems may be manual, semi-automated or completely automated. The BACTEC system (from Becton Dickinson) and the

10

15

20

25

30

35

BacTAlert system (from Organon Teknika Corporation) are the two most widely used automated blood culture systems. These systems incubate blood culture bottles under optimal conditions for bacterial growth. Bacterial growth is monitored continuously to detect early positives by using highly sensitive bacterial growth detectors. Once growth is detected, a Gram stain is performed directly from the blood culture and then used to inoculate nutrient agar plates. Subsequently, bacterial identification and susceptibility testing are carried out from isolated bacterial colonies with automated systems as described previously. The bottles are normally reported as negative if no growth is detected after an incubation of 6 to 7 days. Normally, the vast majority of blood cultures are reported negative. For example, the percentage of negative blood cultures at the microbiology laboratory of the CHUL for the period February 1994–January 1995 was 93.1% (Table 3).

Other clinical samples

Upon receipt by the clinical microbiology laboratory, all body fluids other than blood and urine that are from normally sterile sites (i.e. cerebrospinal, synovial, pleural, pericardial and others) are processed for direct microscopic examination and subsequent culture. Again, most clinical samples are negative for culture (Table 3).

Regarding clinical specimens which are not from sterile sites such as sputum or stool specimens, the laboratory diagnosis by culture is more problematic because of the contamination by the normal flora. The bacterial pathogens potentially associated with the infection are purified from the contaminants and then identified as described previously. Of course, the universal detection of bacteria would not be useful for the diagnosis of bacterial infections at these non sterile sites. On the other hand, DNA-based assays for species or genus detection and identification as well as for the detection of antibiotic resistance genes from these specimens would be very useful and would offer several advantages over classical identification and susceptibility testing methods.

DNA-based assays with any clinical specimens

There is an obvious need for rapid and accurate diagnostic tests for bacterial detection and identification directly from clinical specimens. DNA-based technologies are rapid and accurate and offer a great potential to improve the diagnosis of infectious diseases (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). The DNA probes and amplification primers which are objects of the present invention are applicable for bacterial or fungal detection and identification directly from any clinical specimens such as blood cultures, blood, urine, sputum, cerebrospinal fluid, pus and other type of specimens (Table 3). The DNA-based tests proposed in this invention are superior in terms of both rapidity and accuracy to standard biochemical methods currently used for routine diagnosis from any clinical specimens in microbiology laboratories. Since

10

15

20

25

30

35

these tests are performed in around only one hour, they provide the clinicians with new diagnostic tools which should contribute to increase the efficiency of therapies with antimicrobial agents. Clinical specimens from organisms other than humans (e.g. other primates, birds, plants, mammals, farm animals, livestock and others) may also be tested with these assays.

A high percentage of culture negative specimens

Among all the clinical specimens received for routine diagnosis, approximately 80% of urine specimens and even more (around 95%) for other types of clinical specimens are negative for the presence of bacterial pathogens (Table 3). It would also be desirable, in addition to identify bacteria at the species or genus level in a given specimen, to screen out the high proportion of negative clinical specimens with a test detecting the presence of any bacterium (i.e. universal bacterial detection). Such a screening test may be based on the DNA amplification by PCR of a highly conserved genetic target found in all bacteria. Specimens negative for bacteria would not be amplified by this assay. On the other hand, those that are positive for bacteria would give a positive amplification signal with this assay.

Towards the development of rapid DNA-based diagnostic tests

A rapid diagnostic test should have a significant impact on the management of infections. DNA probe and DNA amplification technologies offer several advantages over conventional methods for the identification of pathogens and antibiotic resistance genes from clinical samples (Persing et al., 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.; Ehrlich and Greenberg, 1994, PCR-based Diagnostics in Infectious Disease, Blackwell Scientific Publications, Boston, MA). There is no need for culture of the bacterial pathogens, hence the organisms can be detected directly from clinical samples, thereby reducing the time associated with the isolation and identification of pathogens. Furthermore, DNA-based assays are more accurate for bacterial identification than currently used phenotypic identification systems which are based on biochemical tests. Commercially available DNA-based technologies are currently used in clinical microbiology laboratories, mainly for the detection and identification of fastidious bacterial pathogens such as Mycobacterium tuberculosis, Chlamydia trachomatis, Neisseria gonorrhoeae as well as for the detection of a variety of viruses (Podzorski and Persing, Molecular detection and identification of microorganisms, In: P. Murray et al., 1995, Manual of Clinical Microbiology, ASM press, Washington D.C.). There are also other commercially available DNA-based assays which are used for culture confirmation assays.

Others have developed DNA-based tests for the detection and identification of bacterial pathogens which are objects of the present invention: *Staphylococcus* spp. (US patent application serial No. US 5 437 978), *Neisseria* spp. (US patent application

10

15

20

25

30

35

serial No. US 5 162 199 and European patent application serial No. EP 0 337 896 131) and *Listeria monocytogenes* (US patent applications serial Nos US 5 389 513 and US 5 089 386). However, the diagnostic tests described in these patents are based either on rRNA genes or on genetic targets different from those described in the present invention.

Although there are diagnostic kits or methods already used in clinical microbiology laboratories, there is still a need for an advantageous alternative to the conventional culture identification methods in order to improve the accuracy and the speed of the diagnosis of commonly encountered bacterial infections. Besides being much faster, DNA-based diagnostic tests are more accurate than standard biochemical tests presently used for diagnosis because the bacterial genotype (e.g. DNA level) is more stable than the bacterial phenotype (e.g. metabolic level).

Knowledge of the genomic sequences of bacterial and fungal species continuously increases as testified by the number of sequences available from databases. From the sequences readily available from databases, there is no indication therefrom as to their potential for diagnostic purposes. For determining good candidates for diagnostic purposes, one could select sequences for DNA-based assays for (i) the species-specific detection and identification of commonly encountered bacterial or fungal pathogens, (ii) the genus-specific detection and identification of commonly encountered bacterial or fungal pathogens, (iii) the universal detection of bacterial or fungal pathogens and/or (iv) the specific detection and identification of antibiotic resistance genes. All of the above types of DNA-based assays may be performed directly from any type of clinical specimens or from a microbial culture.

In our co-pending U.S. (N.S. 08/526,840) and PCT (PCT/CA/95/00528) patent applications, we described DNA sequences suitable for (i) the species-specific detection and identification of 12 clinically important bacterial pathogens, (ii) the universal detection of bacteria, and (iii) the detection of 17 antibiotic resistance genes. This co-pending application described proprietary DNA sequences and DNA sequences selected from databases (in both cases, fragments of at least 100 base pairs), as well as oligonucleotide probes and amplification primers derived from these sequences. All the nucleic acid sequences described in this patent application enter the composition of diagnostic kits and methods capable of a) detecting the presence of bacteria, b) detecting specifically the presence of 12 bacterial species and 17 antibiotic resistance genes. However, these methods and kits need to be improved, since the ideal kit and method should be capable of diagnosing close to 100% of microbial pathogens and antibiotic resistance genes. For example, infections caused by *Enterococcus faecium* have become a clinical problem because of its resistance to many antibiotics. Both the detection of these bacteria and the evaluation of their

resistance profiles are desirable. Besides that, novel DNA sequences (probes and primers) capable of recognizing the same and other microbial pathogens or the same and additional antibiotic resistance genes are also desirable to aim at detecting more target genes and complement our earlier patent application.

5

STATEMENT OF THE INVENTION

It is an object of the present invention to provide a specific, ubiquitous and sensitive method using probes and/or amplification primers for determining the presence and/or amount of nucleic acids:

10

- from specific microbial species or genera selected from the group consisting of *Streptococcus* species, *Streptococcus* agalactiae, *Staphylococcus* species, *Staphylococcus* saprophyticus, *Enterococcus* species, *Enterococcus* faecium, *Neisseria* species, *Neisseria* meningitidis, *Listeria* monocytogenes, *Candida* species and *Candida* albicans

15

20

25

- from an antibiotic resistance gene selected from the group consisting of bla_{tem} , bla_{rob} , bla_{shv} , bla_{oxa} , bla_{ox

- from any bacterial species

in any sample suspected of containing said nucleic acids,

wherein each of said nucleic acids or a variant or part thereof comprises a selected target region hybridizable with said probe or primers;

said method comprising the steps of contacting said sample with said probes or primers and detecting the presence and/or amount of hybridized probes or amplified products as an indication of the presence and/or amount of said any bacterial species, specific microbial species or genus and antibiotic resistance gene.

In a specific embodiment, a similar method directed to each specific microbial species or genus detection and identification, antibiotic resistance genes detection, and universal bacterial detection, separately, is provided.

30

In a more specific embodiment, the method makes use of DNA fragments (proprietary fragments and fragments obtained from databases), selected for their capacity to sensitively, specifically and ubiquitously detect the targeted bacterial or fungal nucleic acids.

35

In a particularly preferred embodiment, oligonucleotides of at least 12 nucleotides in length have been derived from the longer DNA fragments, and are used in the present method as probes or amplification primers.

The proprietary oligonucleotides (probes and primers) are also another object of the invention.

Diagnostic kits comprising probes or amplification primers for the detection of

a microbial species or genus selected from the group consisting of *Streptococcus* species, *Streptococcus* agalactiae, *Staphylococcus* species, *Staphylococcus* saprophyticus, *Enterococcus* species, *Enterococcus* faecium, *Neisseria* species, *Neisseria meningitidis*, *Listeria monocytogenes*, *Candida* species and *Candida* albicans are also objects of the present invention.

Diagnostic kits further comprising probes or amplification primers for the detection of an antibiotic resistance gene selected from the group consisting of bla_{tem} , bla_{rob} , bla_{shv} , bla_{oxa} , blaZ, aadB, aacC1, aacC2, aacC3, aacA4, aac6'-IIa, ermA, ermB, ermC, mecA, vanA, vanB, vanC, satA, aac(6')-aph(2''), aad(6'), vat, vga, msrA, sul and int are also objects of this invention.

Diagnostic kits further comprising probes or amplification primers for the detection of any bacterial or fungal species, comprising or not comprising those for the detection of the specific microbial species or genus listed above, and further comprising or not comprising probes and primers for the antibiotic resistance genes listed above, are also objects of this invention.

In a preferred embodiment, such a kit allows for the separate or the simultaneous detection and identification of the above-listed microbial species or genus, antibiotic resistance genes and for the detection of any bacterium.

In the above methods and kits, amplification reactions may include a) polymerase chain reaction (PCR), b) ligase chain reaction, c) nucleic acid sequence-based amplification, d) self-sustained sequence replication, e) strand displacement amplification, f) branched DNA signal amplification, g) transcription-mediated amplification, h) cycling probe technology (CPT) i) nested PCR, or j) multiplex PCR.

In a preferred embodiment, a PCR protocol is used as an amplification reaction.

In a particularly preferred embodiment, a PCR protocol is provided, comprising, for each amplification cycle, an annealing step of 30 seconds at 45-55°C and a denaturation step of only one second at 95°C, without any time allowed specifically for the elongation step. This PCR protocol has been standardized to be suitable for PCR reactions with all selected primer pairs, which greatly facilitates the testing because each clinical sample can be tested with universal, species-specific, genus-specific and antibiotic resistance gene PCR primers under uniform cycling conditions. Furthermore, various combinations of primer pairs may be used in multiplex PCR assays.

We aim at developing a rapid test or kit to discard rapidly all the samples which are negative for bacterial cells and to subsequently detect and identify the above bacterial and/or fungal species and genera and to determine rapidly the bacterial resistance to antibiotics. Although the sequences from the selected antibiotic resistance genes are available from databases and have been used to develop DNA-based tests for their detection, our approach is unique because it represents a major improvement over current gold standard diagnostic methods based on bacterial

35

5

10

15

20

25

30

cultures. Using an amplification method for the simultaneous bacterial detection and identification and antibiotic resistance genes detection, there is no need for culturing the clinical sample prior to testing. Moreover, a modified PCR protocol has been developed to detect all target DNA sequences in approximately one hour under uniform amplification conditions. This procedure will save lives by optimizing treatment, will diminish antibiotic resistance because less antibiotics will be prescribed, will reduce the use of broad spectrum antibiotics which are expensive, decrease overall health care costs by preventing or shortening hospitalizations, and decrease the time and costs associated with clinical laboratory testing.

10

5

In the methods and kits described herein below, the oligonucleotide probes and amplification primers have been derived from larger sequences (i.e. DNA fragments of at least 100 base pairs). All DNA fragments have been obtained either from proprietary fragments or from databases. DNA fragments selected from databases are newly used in a method of detection according to the present invention, since they have been selected for their diagnostic potential.

15

20

25

30

35

It is clear to the individual skilled in the art that other oligonucleotide sequences appropriate for (i) the universal bacterial detection, (ii) the detection and identification of the above microbial species or genus and (iii) the detection of antibiotic resistance genes other than those listed in Annex VI may also be derived from the proprietary fragments or selected database sequences. For example, the oligonucleotide primers or probes may be shorter or longer than the ones we have chosen; they may also be selected anywhere else in the proprietary DNA fragments or in the sequences selected from databases; they may be also variants of the same oligonucleotide. If the target DNA or a variant thereof hybridizes to a given oligonucleotide, or if the target DNA or a variant thereof can be amplified by a given oligonucleotide PCR primer pair, the converse is also true; a given target DNA may hybridize to a variant oligonucleotide probe or be amplified by a variant oligonucleotide PCR primer. Alternatively, the oligonucleotides may be designed from any DNA fragment sequences for use in amplification methods other than PCR. Consequently, the core of this invention is the identification of universal, species-specific, genus-specific and resistance gene-specific genomic or non-genomic DNA fragments which are used as a source of specific and ubiquitous oligonucleotide probes and/or amplification primers. Although the selection and evaluation of oligonucleotides suitable for diagnostic purposes requires much effort, it is quite possible for the individual skilled in the art to derive, from the selected DNA fragments, oligonucleotides other than the ones listed in Annex VI which are suitable for diagnostic purposes. When a proprietary fragment or a database sequence is selected for its specificity and ubiquity, it increases the probability that subsets thereof will also be specific and ubiquitous.

Since a high percentage of clinical specimens are negative for bacteria (Table

10

15

20

25

30

35

3), DNA fragments having a high potential for the selection of universal oligonucleotide probes or primers were selected from proprietary and database sequences. The amplification primers were selected from a gene highly conserved in bacteria and fungi, and are used to detect the presence of any bacterial pathogen in clinical specimens in order to determine rapidly (approximately one hour) whether it is positive or negative for bacteria. The selected gene, designated tuf, encodes a protein (EF-Tu) involved in the translational process during protein synthesis. The tuf gene sequence alignments used to derive the universal primers include both proprietary and database sequences (Example 1 and Annex I). This strategy allows the rapid screening of the numerous negative clinical specimens (around 80% of the specimens received, see Table 3) submitted for bacteriological testing. Tables 4, 5 and 6 provide a list of the bacterial or fungal species used to test the specificity of PCR primers and DNA probes. Table 7 gives a brief description of each species-specific, genus-specific and universal amplification assays which are objects of the present invention. Tables 8, 9 and 10 provide some relevant information about the proprietary and database sequences selected for diagnostic puposes.

DETAILED DESCRIPTION OF THE INVENTION

Development of species-specific, genus-specific, universal and antibiotic resistance gene-specific DNA probes and amplification primers for microorganisms

Selection from databases of sequences suitable for diagnostic purposes

In order to select sequences which are suitable for species-specific or genusspecific detection and identification of bacteria or fungi or, alternatively, for the universal detection of bacteria, the database sequences (GenBank, EMBL and Swiss-Prot) were chosen based on their potential for diagnostic purposes according to sequence information and computer analysis performed with these sequences. Initially, all sequence data available for the targeted microbial species or genus were carefully analyzed. The gene sequences which appeared the most promising for diagnostic purposes based on sequence information and on sequence comparisons with the corresponding gene in other microbial species or genera performed with the Genetics Computer Group (GCG, Wisconsin) programs were selected for testing by PCR. Optimal PCR amplification primers were chosen from the selected database sequences with the help of the Oligo™ 4.0 primer analysis software (National Biosciences Inc., Plymouth, Minn.). The chosen primers were tested in PCR assays for their specificity and ubiquity for the target microbial species or genus. In general, the identification of database sequences from which amplification primers suitable for species-specific or genus-specific detection and identification were selected involved the computer analysis and PCR testing of several candidate gene sequences before

10

15

20

25

30

35

obtaining a primer pair which is specific and ubiquitous for the target microbial species or genus. Annex VI provides a list of selected specific and ubiquitous PCR primer pairs. Annexes I to V and Examples 1 to 4 illustrate the strategy used to select genus-specific, species-specific and universal PCR primers from *tuf* sequences or from the *rec*A gene.

Oligonucleotide primers and probes design and synthesis

The DNA fragments sequenced by us or selected from databases (GenBank and EMBL) were used as sources of oligonucleotides for diagnostic purposes. For this strategy, an array of suitable oligonucleotide primers or probes derived from a variety of genomic DNA fragments (size of more than 100 bp) selected from databases were tested for their specificity and ubiquity in PCR and hybridization assays as described later. It is important to note that the database sequences were selected based on their potential for being species-specific, genus-specific or universal for the detection of bacteria or fungi according to available sequence information and extensive analysis and that, in general, several candidate database sequences had to be tested in order to obtain the desired specificity, ubiquity and sensitivity.

Oligonucleotide probes and amplification primers derived from species-specific fragments selected from database sequences were synthesized using an automated DNA synthesizer (Perkin-Elmer Corp., Applied Biosystems Division). Prior to synthesis, all oligonucleotides (probes for hybridization and primers for DNA amplification) were evaluated for their suitability for hybridization or DNA amplification by polymerase chain reaction (PCR) by computer analysis using standard programs (i.e. the Genetics Computer Group (GCG) programs and the primer analysis software OligoTM 4.0). The potential suitability of the PCR primer pairs was also evaluated prior to the synthesis by verifying the absence of unwanted features such as long stretches of one nucleotide and a high proportion of G or C residues at the 3' end (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.).

The oligonucleotide primers or probes may be derived from either strand of the duplex DNA. The primers or probes may consist of the bases A, G, C, or T or analogs and they may be degenerated at one or more chosen nucleotide position(s). The primers or probes may be of any suitable length and may be selected anywhere within the DNA sequences from proprietary fragments or from selected database sequences which are suitable for (i) the universal detection of bacteria, (ii) the species-specific detection and identification of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae* and *Candida albicans* (iii) the genus-specific detection of *Streptococcus* species, *Enterococcus* species, *Staphylococcus* species and *Neisseria* species or (iv) the detection of the 26 above-mentioned clinically important antibiotic resistance genes.

10

15

20

25

30

35

Variants for a given target bacterial gene are naturally occurring and are attributable to sequence variation within that gene during evolution (Watson et al., 1987, Molecular Biology of the Gene, 4th ed., The Benjamin/Cummings Publishing Company, Menlo Park, CA; Lewin, 1989, Genes IV, John Wiley & Sons, New York. NY). For example, different strains of the same bacterial species may have a single or more nucleotide variation(s) at the oligonucleotide hybridization site. The person skilled in the art is well aware of the existence of variant bacterial or fungal DNA sequences for a specific gene and that the frequency of sequence variations depends on the selective pressure during evolution on a given gene product. The detection of a variant sequence for a region between two PCR primers may be demonstrated by sequencing the amplification product. In order to show the presence of sequence variants at the primer hybridization site, one has to amplify a larger DNA target with PCR primers outside that hybridization site. Sequencing of this larger fragment will allow the detection of sequence variation at this site. A similar strategy may be applied to show variants at the hybridization site of a probe. Insofar as the divergence of the target sequences or a part thereof does not affect the specificity and ubiquity of the amplification primers or probes, variant bacterial DNA is under the scope of this invention. Variants of the selected primers or probes may also be used to amplify or hybridize to a variant DNA.

Sequencing of tuf sequences from a variety of bacterial and fungal species

The nucleotide sequence of a portion of tuf genes was determined for a variety of bacterial and fungal species. The amplification primers SEQ ID NOs: 107 and 108, which amplify a tuf gene portion of approximately 890 bp, were used for the sequencing of bacterial tuf sequences. The amplification primers SEQ ID NOs: 109 and 172, which amplify a tuf gene portion of approximately 830 bp, were used for the sequencing of fungal tuf sequences. Both primer pairs can amplify tufA and tufB genes. This is not surprising because these two genes are nearly identical. For example, the entire tufA and tufB genes from E. coli differ at only 13 nucleotide positions (Neidhardt et al., 1996, Escherichia coli and Salmonella: Cellular and Molecular Biology, 2nd ed., American Society for Microbiology Press, Washington, D.C.). These amplification primers are degenerated at several nucleotide positions and contain inosines in order to allow the amplification of a wide range of tuf sequences. The strategy used to select these amplification primers is similar to that illustrated in Annex I for the selection of universal primers. The amplification primers SEQ ID NOs: 107 and 108 could be used to amplify the tuf genes from any bacterial species. The amplification primers SEQ ID NOs: 109 and 172 could be used to amplify the tuf genes from any fungal species.

The *tuf* genes were amplified directly from bacterial or yeast cultures using the following amplification protocol: One μ L of cell suspension was transferred directly to

10

15

20

25

30

35

19 μ L of a PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl₂, 1 μ M of each of the 2 primers, 200 μ M of each of the four dNTPs, 0.5 unit of Taq DNA polymerase (Promega Corp., Madison, WI). PCR reactions were subjected to cycling using a MJ Research PTC-200 thermal cycler (MJ Research Inc., Watertown, Mass.) as follows: 3 min at 96°C followed by 30-35 cycles of 1 min at 95°C for the denaturation step, 1 min at 30-50°C for the annealing step and 1 min at 72°C for the extension step. Subsequently, twenty microliters of the PCRamplified mixture were resolved by electrophoresis in a 1.5% agarose gel. The gel was then visualized by staining with methylene blue (Flores et al., 1992, Biotechniques, 13:203-205). The size of the amplification products was estimated by comparison with a 100-bp molecular weight ladder. The band corresponding to the specific amplification product (i.e. approximately 890 or 830 bp for bacterial or fungal tuf sequences, respectively) was excised from the agarose gel and purified using the QlAquick™ gel extraction kit (QIAGEN Inc., Chatsworth, CA). The gel-purified DNA fragment was then used directly in the sequencing protocol. Both strands of the tuf genes amplification product were sequenced by the dideoxynucleotide chain termination sequencing method by using an Applied Biosystems automated DNA sequencer (model 373A) with their PRISM™ Sequenase® Terminator Double-stranded DNA Sequencing Kit (Perkin-Elmer Corp., Applied Biosystems Division, Foster City, CA). The sequencing reactions were all performed by using the amplification primers (SEQ ID NOs: 107 to 109 and 172) and 100 ng per reaction of the gel-purified amplicon. In order to ensure that the determined sequence did not contain errors attributable to the sequencing of PCR artefacts, we have sequenced two preparations of the gel-purified tuf amplification product originating from two independent PCR amplifications. For all target microbial species, the sequences determined for both amplicon preparations were identical. Furthermore, the sequences of both strands were 100% complementary thereby confirming the high accuracy of the determined sequence. The tuf sequences determined using the above strategy are all in the Sequence Listing (i.e. SEQ ID NOs:118 to 146). Table 13 gives the originating microbial species and the source for each tuf sequence in the Sequence Listing.

The alignment of the *tuf* sequences determined by us or selected from databases reveals clearly that the length of the sequenced portion of the *tuf* genes is variable. There may be insertions or deletions of several amino acids. This explains why the size of the sequenced *tuf* amplification product was variable for both bacterial and fungal species. Among the *tuf* sequences determined by our group, we found insertions and deletions adding up to 5 amino acids or 15 nucleotides. Consequently, the nucleotide positions indicated on top of each of Annexes I to V do not correspond for *tuf* sequences having insertions or deletions.

It should also be noted that the various tuf sequences determined by us

10

15

20

25

30

35

occasionally contain degenerescences. These degenerated nucleotides correspond to sequence variations between *tufA* and *tufB* genes because the amplification primers amplify both *tuf* genes. These nucleotide variations were not attributable to nucleotide misincorporations by the *taq* DNA polymerase because the sequence of both strands were identical and also because the sequences determined with both preparations of the gel-purified *tuf* amplicons were identical.

The selection of amplification primers from tuf sequences

The *tuf* sequences determined by us or selected from databases were used to select PCR primers for (i) the universal detection of bacteria, (ii) the genus-specific detection and identification of *Enterococcus* spp. and *Staphylococcus* spp. and (iii) the species-specific detection and identification of *Candida albicans*. The strategy used to select these PCR primers was based on the analysis of multiple sequence alignments of various *tuf* sequences. For more details about the selection of PCR primers from *tuf* sequences, please refer to Examples 1 to 3 and Annexes I to IV.

The selection of amplification primers from recA

The comparison of the nucleotide sequence for the *recA* gene from various bacterial species including 5 species of streptococci allowed the selection of *Streptococcus*-specific PCR primers. For more details about the selection of PCR primers from *recA*, please refer to Example 4 and Annex V.

DNA fragment isolation from Staphylococcus saprophyticus by arbitrarily primed PCR

DNA sequences of unknown coding potential for the species-specific detection and identification of *Staphylococcus saprophyticus* were obtained by the method of arbitrarily primed PCR (AP-PCR).

AP-PCR is a method which can be used to generate specific DNA probes for microorganisms (Fani *et al.*, 1993, Mol. Ecol. **2**:243-250). A description of the AP-PCR protocol used to isolate a species-specific genomic DNA fragment from *Staphylococcus saprophyticus* follows. Twenty different oligonucleotide primers of 10 nucleotides in length (all included in the AP-PCR kit OPAD (Operon Technologies, Inc., Alameda, CA)) were tested systematically with DNAs from 3 bacterial strains of *Staphylococcus saprophyticus* (all obtained from the American Type Culture Collection (ATCC): numbers 15305, 35552 and 43867) as well as with DNA from four other staphylococcul species (*Staphylococcus aureus* ATCC 25923, *Staphylococcus epidermidis* ATCC 14990, *Staphylococcus haemolyticus* ATCC 29970 and *Staphylococcus hominis* ATCC 35982). For all bacterial species, amplification was performed from a bacterial suspension adjusted to a standard 0.5 McFarland which corresponds to approximately 1.5 x 10^8 bacteria/mL. One μ L of the standardized bacterial suspension was transferred directly to 19μ L of a PCR reaction mixture containing 50 mM KCl, 10μ Cl, 10μ C

 $1.2~\mu\text{M}$ of only one of the 20 different AP-PCR primers OPAD, 200 μM of each of the four dNTPs and 0.5 unit of Taq DNA polymerase (Promega Corp., Madison, WI). PCR reactions were subjected to cycling using a MJ Research PTC-200 thermal cycler (MJ Research Inc.) as follows: 3 min at 96°C followed by 35 cycles of 1 min at 95°C for the denaturation step, 1 min at 32°C for the annealing step and 1 min at 72°C for the extension step. A final extension step of 7 min at 72°C was made after the 35 cycles to ensure complete extension of PCR products. Subsequently, twenty microliters of the PCR amplified mixture were resolved by electrophoresis in a 2% agarose gel containing 0.25 μ g/mL of ethidium bromide. The size of the amplification products was estimated by comparison with a 50-bp molecular weight ladder.

5

10

15

20

25

30

35

Amplification patterns specific for *Staphylococcus saprophyticus* were observed with the AP-PCR primer OPAD-9 (SEQ ID NO: 25). Amplification with this primer consistently showed a band corresponding to a DNA fragment of approximately 450 bp for all *Staphylococcus saprophyticus* strains tested but not for any of the four other staphylococcal species tested. This species-specific pattern was confirmed by testing 10 more clinical isolates of *S. saprophyticus* selected from the culture collection of the microbiology laboratory of the CHUL as well as strains selected from the gram-positive bacterial species listed in Table 5.

The band corresponding to the approximately 450 bp amplicon which was specific and ubiquitous for *S. saprophyticus* based on AP-PCR was excised from the agarose gel and purified using the QIAquickTM gel extraction kit (QIAGEN Inc.). The gel-purified DNA fragment was cloned into the T/A cloning site of the pCR 2.1TM plasmid vector (Invitrogen Inc.) using T4 DNA ligase (New England BioLabs). Recombinant plasmids were transformed into *E. coli* DH5α competent cells using standard procedures. Plasmid DNA isolation was done by the method of Birnboim and Doly (Nucleic Acids Res. 7:1513-1523) for small-scale preparations. All plasmid DNA preparations were digested with the *Eco*RI restriction endonuclease to ensure the presence of the approximately 450 bp AP-PCR insert into the recombinant plasmids. Subsequently, a large-scale and highly purified plasmid DNA preparation was performed from two selected clones shown to carry the AP-PCR insert by using the QIAGEN plasmid purification kit. These plasmid preparations were used for automated DNA sequencing.

Both strands of the AP-PCR insert from the two selected clones were sequenced by the dideoxynucleotide chain termination sequencing method with SP6 and T7 sequencing primers, by using an Applied Biosystems automated DNA sequencer as described previously. The analysis of the obtained sequences revealed that the DNA sequences for both strands from each clone were 100% complementary. Furthermore, it showed that the entire sequence determined for each clone were both identical. These sequencing data confirm the 100% accuracy for the determined 438

10

15

20

25

30

35

bp sequence (SEQ ID NO: 29). Optimal amplification primers have been selected from the sequenced AP-PCR *Staphylococcus saprophyticus* DNA fragment with the help of the primer analysis software Oligo™ 4.0. The selected primer sequences have been tested in PCR assays to verify their specificity and ubiquity (Table 7). These PCR primers were specific since there was no amplification with DNA from bacterial species other than *S. saprophyticus* selected from Tables 4 and 5. Furthermore, this assay was ubiquitous since 245 of 260 strains of *S. saprophyticus* were efficiently amplified with this PCR assay. When used in combination with another *S. saprophyticus*-specific PCR assay, which is an object of our co-pending U.S. (N.S. 08/526,840) and PCT (PCT/CA/95/00528) patent applications, the ubiquity reaches 100% for these 260 strains.

DNA amplification

For DNA amplification by the widely used PCR (polymerase chain reaction) method, primer pairs were derived from proprietary DNA fragments or from database sequences. Prior to synthesis, the potential primer pairs were analyzed by using the OligoTM 4.0 software to verify that they are good candidates for PCR amplification.

During DNA amplification by PCR, two oligonucleotide primers binding respectively to each strand of the heat-denatured target DNA from the bacterial genome are used to amplify exponentially *in vitro* the target DNA by successive thermal cycles allowing denaturation of the DNA, annealing of the primers and synthesis of new targets at each cycle (Persing *et al*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.).

Briefly, the PCR protocols were as follow: Treated clinical specimens or standardized bacterial or fungal suspensions (see below) were amplified in a 20 µL PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 2.5 mM MgCl₂, 0.4 μ M of each primer, 200 μ M of each of the four dNTPs and 0.5 unit of Tag DNA polymerase (Promega) combined with the TagStart™ antibody (Clontech Laboratories Inc., Palo Alto, CA). The TagStart™ antibody, which is a neutralizing monoclonal antibody to Tag DNA polymerase, was added to all PCR reactions to enhance the specificity and the sensitivity of the amplifications (Kellogg et al., 1994, Biotechniques 16:1134-1137). The treatment of the clinical specimens varies with the type of specimen tested, since the composition and the sensitivity level required are different for each specimen type. It consists in a rapid protocol to lyse the bacterial cells and eliminate the PCR inhibitory effects (see example 11 for urine specimen preparation). For amplification from bacterial or fungal cultures, the samples were added directly to the PCR amplification mixture without any pre-treatment step (see example 10). Primer sequences derived from highly conserved regions of the bacterial 16S ribosomal RNA gene were used to provide an internal control for all PCR reactions. Alternatively, the

10

15

20

25

30

35

internal control was derived from sequences not found in microorganisms or in the human genome. The internal control was integrated into all amplification reactions to verify the efficiency of the PCR assays and to ensure that significant PCR inhibition was absent. The internal control derived from rRNA was also useful to monitor the efficiency of bacterial lysis protocols.

PCR reactions were then subjected to thermal cycling (3 min at 95°C followed by 30 cycles of 1 second at 95°C for the denaturation step and 30 second at 55°C for the annealing-extension step) using a PTC-200 thermal cycler (MJ Research Inc.) and subsequently analyzed by standard ethidium bromide-stained agarose gel electrophoresis. The number of cycles performed for the PCR assays varies according to the sensitivity level required. For example, the sensitivity level required for microbial detection directly from clinical specimens is higher for blood specimens than for urine specimens because the concentration of microorganisms associated with a septicemia can be much lower than that associated with a urinary tract infection. Consequently, more sensitive PCR assays having more thermal cycles are required for direct detection from blood specimens. Similarly, PCR assays performed directly from bacterial or fungal cultures may be less sensitive than PCR assays performed directly from clinical specimens because the number of target organisms is normally much lower in clinical specimens than in microbial cultures.

It is clear that other methods for the detection of specific amplification products, which may be faster and more practical for routine diagnosis, may be used. Such methods may be based on the detection of fluorescence after amplification (e.g. TaqMan™ system from Perkin Elmer or Amplisensor™ from Biotronics). Methods based on the detection of fluorescence are particularly promising for utilization in routine diagnosis as they are very rapid, quantitative and can be automated (Example 14).

Microbial pathogens detection and identification may also be performed by solid support or liquid hybridization using species-specific internal DNA probes hybridizing to an amplification product. Such probes may be generated from any species-specific or genus-specific DNA amplification products which are objects of the present invention. Alternatively, the internal probes for species or genus detection and identification may be derived from the amplicons produced by the universal amplification assay. The oligonucleotide probes may be labeled with biotin or with digoxigenin or with any other reporter molecules.

To assure PCR efficiency, glycerol, dimethyl sulfoxide (DMSO) or other related solvents can be used to increase the sensitivity of the PCR and to overcome problems associated with the amplification of a target DNA having a high GC content or forming strong secondary structures (Dieffenbach and Dveksler, 1995, PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, New York). The

10

15

20

25

30

35

concentration ranges for glycerol and DMSO are 5-15% (v/v) and 3-10% (v/v), respectively. For the PCR reaction mixture, the concentration ranges for the amplification primers and $MgCl_2$ are 0.1-1.5 μ M and 1.5-3.5 mM, respectively. Modifications of the standard PCR protocol using external and nested primers (i.e. nested PCR) or using more than one primer pair (i.e. multiplex PCR) may also be used (Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). For more details about the PCR protocols and amplicon detection methods, see Examples 9 to 14.

The person skilled in the art of DNA amplification knows the existence of other rapid amplification procedures such as ligase chain reaction (LCR), transcription-mediated amplification (TMA), self-sustained sequence replication (3SR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA), branched DNA (bDNA) and cycling probe technology (CPT) (Lee *et al.*, 1997, Nucleic Acid Amplification Technologies: Application to Disease Diagnosis, Eaton Publishing, Boston, MA; Persing *et al.*, 1993, Diagnostic Molecular Microbiology: Principles and Applications, American Society for Microbiology, Washington, D.C.). The scope of this invention is not limited to the use of amplification by PCR, but rather includes the use of any rapid nucleic acid amplification method or any other procedure which may be used to increase rapidity and sensitivity of the tests. Any oligonucleotide suitable for the amplification of nucleic acids by approaches other than PCR and derived from the species-specific, genus-specific and universal DNA fragments as well as from selected antibiotic resistance gene sequences included in this document are also under the scope of this invention.

Hybridization assays with oligonucleotide probes

In hybridization experiments, single-stranded oligonucleotides (size less than 100 nucleotides) have some advantages over DNA fragment probes for the detection of bacteria, such as ease of synthesis in large quantities, consistency in results from batch to batch and chemical stability. Briefly, for the hybridizations, oligonucleotides were 5' end-labeled with the radionucleotide γ-32P(dATP) using T4 polynucleotide kinase (Pharmacia) (Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). The unincorporated radionucleotide was removed by passing the labeled oligonucleotide through a Sephadex G-50TM column. Alternatively, oligonucleotides were labeled with biotin, either enzymatically at their 3' ends or incorporated directly during synthesis at their 5' ends, or with digoxigenin. It will be appreciated by the person skilled in the art that labeling means other than the three above labels may be used.

Each oligonucleotide probe was then tested for its specificity by hybridization to DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6. All of the bacterial or fungal species tested were likely to be pathogens associated

10

15

20

25

30

35

with common infections or potential contaminants which can be isolated from clinical specimens. Each target DNA was released from bacterial cells using standard chemical treatments to lyse the cells (Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Subsequently, the DNA was denatured by conventional methods and then irreversibly fixed onto a solid support (e.g. nylon or nitrocellulose membranes) or free in solution. The fixed single-stranded target DNAs were then hybridized with the oligonucleotide probe cells (Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Prehybridization conditions were in 1 M NaCl + 10% dextran sulfate + 1% SDS + 100 μg/mL salmon sperm DNA at 65°C for 15 min. Hybridization was performed in fresh pre-hybridization solution containing the labeled probe at 65°C overnight. Posthybridization washing conditions were as follows: twice in 3X SSC containing 1% SDS, twice in 2X SSC containing 1% SDS and twice in 1X SSC containing 1% SDS (all of these washes were at 65°C for 15 min), and a final wash in 0.1X SSC containing 1% SDS at 25°C for 15 min. Autoradiography of washed filters allowed the detection of selectively hybridized probes. Hybridization of the probe to a specific target DNA indicated a high degree of similarity between the nucleotide sequence of these two DNAs because of the high stringency of the washes.

An oligonucleotide probe was considered specific only when it hybridized solely to DNA from the species or genus from which it was isolated. Oligonucleotide probes found to be specific were subsequently tested for their ubiquity (i.e. ubiquitous probes recognized most or all isolates of the target species or genus) by hybridization to microbial DNAs from clinical isolates of the species or genus of interest including ATCC strains. The DNAs from strains of the target species or genus were denatured, fixed onto nylon membranes and hybridized as described above. Probes were considered ubiquitous when they hybridized specifically with the DNA from at least 80% of the isolates of the target species or genus.

Specificity and ubiquity tests for oligonucleotide primers and probes

The specificity of oligonucleotide primers and probes, derived either from the DNA fragments sequenced by us or selected from databases, was tested by amplification of DNA or by hybridization with bacterial or fungal species selected from those listed in Tables 4, 5 and 6, as described in the two previous sections. Oligonucleotides found to be specific were subsequently tested for their ubiquity by amplification (for primers) or by hybridization (for probes) with bacterial DNAs from isolates of the target species or genus. Results for specificity and ubiquity tests with the oligonucleotide primers are summarized in Table 7. The specificity and ubiquity of the PCR assays using the selected amplification primer pairs were tested directly from cultures (see Examples 9 and 10) of bacterial or fungal species.

10

15

20

25

30

35

The various species-specific and genus-specific PCR assays which are objects of the present invention are all specific. For the PCR assays specific to bacterial species or genus, this means that DNA isolated from a wide variety of bacterial species, other than that from the target species or genus and selected from Tables 4 and 5, could not be amplified. For the PCR assay specific to *Candida albicans*, it means there was no amplification with genomic DNA from the fungal species listed in Table 6 as well as with a variety of bacterial species selected from Tables 4 and 5.

The various species-specific and genus-specific PCR assays which are objects of the present invention are also all ubiquitous (Table 7). (i) The species-specific PCR assays for E. faecium, L. monocytogenes, S. saprophyticus, S. agalactiae and C. albicans amplified genomic DNA from all or most strains of the target species tested, which were obtained from various sources and which are representative of the diversity within each target species (Table 7). The species identification of all of these strains was based on classical biochemical methods which are routinely used in clinical microbiology laboratories. (ii) The genus-specific PCR assays specific for Enterococcus spp., Staphylococcus spp., Streptococcus spp. and Neisseria spp. amplified genomic DNA from all or most strains of the target genus tested, which represent all clinically important bacterial species for each target genus. These strains were obtained from various sources and are representative of the diversity within each target genus. Again, the species identification of all of these strains was based on classical biochemical methods which are routinely used in clinical microbiology laboratories. More specifically, the four genus-specific PCR assays amplified the following species: (1) The Enterococcus-specific assay amplified efficiently DNA from all of the 11 enterococcal species tested including E. avium, E. casseliflavus, E. dispar, E. durans, E. faecalis, E. faecium, E. flavescens, E. gallinarum, E. hirae, E. mundtii and E. raffinosus. (2) The Neisseria-specific assay amplified efficiently DNA from all of the 12 neisserial species tested including N. canis, N. cinerea, N. elongata, N. flavescens, N. gonorrhoeae, N. lactamica, N. meningitidis, N. mucosa, N. polysaccharea, N. sicca, N. subflava and N. weaveri. (3) The Staphylococcus-specific assay amplified efficiently DNA from 13 of the 14 staphylococcal species tested S. aureus, S. auricularis, S. capitis, S. cohnii, S. epidermidis, S. including haemolyticus, S. hominis, S. lugdunensis, S. saprophyticus, S. schleiferi, S. simulans, S. warneri and S. xylosus. The staphylococcal species which could not be amplified is S. sciuri. (4) Finally, the Streptococcus-specific assay amplified efficiently DNA from all of the 22 streptococcal species tested including S. agalactiae, S. anginosus, S. bovis, S. constellatus, S. crista, S. dysgalactiae, S. equi, S. gordonii, S. intermedius, S. mitis, S. mutans, S. oralis, S. parasanguis, S. pneumoniae, S. pyogenes, S. salivarius, S. sanguis, S. sabrinus, S. suis, S. uberis, S. vestibularis and S. viridans. On the other hand, the Streptococcus-specific assay did not amplify 3 out of 9 strains

of *S. mutans* and 1 out of 23 strains of *S. salivarius*, thereby showing a slight lack of ubiquity for these two streptococcal species.

All specific and ubiquitous amplification primers for each target microbial species or genus or antibiotic resistance gene investigated are listed in Annex VI. Divergence in the sequenced DNA fragments can occur, insofar as the divergence of these sequences or a part thereof does not affect the specificity of the probes or amplification primers. Variant bacterial DNA is under the scope of this invention.

The PCR amplification primers listed in Annex VI were all tested for their specificity and ubiquity using reference strains as well as clinical isolates from various geographical locations. The 351 reference strains used to test the amplification and hybridization assays (Tables 4, 5 and 6) were obtained from (i) the American Type Culture Collection (ATCC): 85%, (ii) the Laboratoire de santé publique du Québec (LSPQ): 10%, (iii) the Centers for Disease Control and Prevention (CDC): 3%, (iv) the National Culture Type Collection (NCTC): 1% and (v) several other reference laboratories throughout the world: 1%. These reference strains are representative of (i) 90 gram-negative bacterial species (169 strains; Table 4), (ii) 97 gram-positive bacterial species (154 strains; Table 5) and (iii) 12 fungal species (28 strains; Table 6).

Antibiotic resistance genes

5

10

15

20

25

30

35

Antimicrobial resistance complicates treatment and often leads to therapeutic failures. Furthermore, overuse of antibiotics inevitably leads to the emergence of bacterial resistance. Our goal is to provide clinicians, in approximately one hour, the needed information to prescribe optimal treatments. Besides the rapid identification of negative clinical specimens with DNA-based tests for universal bacterial detection and the identification of the presence of a specific pathogen in the positive specimens with species- and/or genus-specific DNA-based tests, clinicians also need timely information about the ability of the bacterial pathogen to resist antibiotic treatments. We feel that the most efficient strategy to evaluate rapidly bacterial resistance to antimicrobials is to detect directly from the clinical specimens the most common and clinically important antibiotic resistance genes (i.e. DNA-based tests for the detection of antibiotic resistance genes). Since the sequence from the most important and common bacterial antibiotic resistance genes are available from databases, our strategy was to use the sequence from a portion or from the entire resistance gene to design specific oligonucleotide primers or probes which will be used as a basis for the development of rapid DNA-based tests. The sequence from each of the bacterial antibiotic resistance genes selected on the basis of their clinical relevance (i.e. high incidence and importance) is given in the Sequence Listing. Tables 9 and 10 summarize some characteristics of the selected antibiotic resistance genes. Our approach is unique because the antibiotic resistance genes detection and the bacterial detection and identification are performed simultaneously in multiplex assays under

uniform PCR amplification conditions (Example 13).

Annex VI provides a list of all amplification primers selected from 26 clinically important antibiotic resistance genes which were tested in PCR assays. The various PCR assays for antibiotic resistance genes detection and identification were validated by testing several resistant bacterial isolates known to carry the targeted gene and obtained from various countries. The testing of a large number of strains which do not carry the targeted resistance gene was also performed to ensure that all assays were specific. So far, all PCR assays for antibiotic resistance genes are highly specific and have detected all control resistant bacterial strains known to carry the targeted gene. The results of some clinical studies to validate the array of PCR assays for the detection and identification of antibiotic resistance genes and correlate these DNA-based assays with standard antimicrobials susceptibility testing methods are presented in Tables 11 and 12.

Universal bacterial detection

15

10

5

In the routine microbiology laboratory, a high percentage of clinical specimens sent for bacterial identification are negative by culture (Table 4). Testing clinical samples with universal amplification primers or universal probes to detect the presence of bacteria prior to specific identification and screen out the numerous negative specimens is thus useful as it saves costs and may rapidly orient the clinical management of the patients. Several amplification primers and probes were therefore synthesized from highly conserved portions of bacterial sequences from the *tuf* genes (Table 8). The universal primer selection was based on a multiple sequence alignment constructed with sequences determined by us or selected from available database sequences as described in Example 1 and Annex I.

25

30

35

20

For the identification of database sequences suitable for the universal detection of bacteria, we took advantage of the fact that the complete genome sequences for two distant microorganisms (i.e. *Mycoplasma genitalium* and *Haemophilus influenzae*) are available. A comparison of the amino acid sequence for all proteins encoded by the genome of these two distant microorganisms led to the identification of highly homologous proteins. An analysis of these homologous proteins allowed to select some promising candidates for the development of universal DNA-based assays for the detection of bacteria. Since the complete nucleotide sequence of several other microbial genomes are presently available in databases, a person skilled in the art could arrive to the same conclusions by comparing genomes sequences other than those of *Mycoplasma genitalium* and *Haemophilus influenzae*. The selected *tuf* gene encodes a protein (EF-Tu) involved in the translation process during protein synthesis. Subsequently, an extensive nucleotide sequence analysis was performed with the *tuf* gene sequences available in databases as well as with novel *tuf* sequences which we have determined as described previously. All computer analysis of amino acid and

10

15

20

25

30

35

nucleotide sequences were performed by using the GCG programs. Subsequently, optimal PCR primers for the universal amplification of bacteria were selected with the help of the Oligo™ program. The selected primers are degenerated at several nucleotide positions and contain several inosines in order to allow the amplification of all clinically relevant bacterial species (Annex I). Inosine is a nucleotide analog able to specifically bind to any of the four nucleotides A, C, G or T. Degenerated oligonucleotides consist of an oligonucleotide mix having two or more of the four nucleotides A, C, G or T at the site of mismatches. The inclusion of inosine and/or of degenerescences in the amplification primers allow mismatch tolerance thereby permitting the amplification of a wider array of target nucleotide sequences (Dieffenbach and Dveksler, 1995 PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, NY).

The amplification conditions with the universal primers were identical to those used for the species- and genus-specific amplification assays except that the annealing temperature was 50°C instead of 55°C. This universal PCR assay was specific and nearly ubiquitous for the detection of bacteria. The specificity for bacteria was verified by amplifying genomic DNA isolated from the 12 fungal species listed in Table 6 as well as genomic DNA from Leishmania donovani, Saccharomyces cerevisiae and human lymphocytes. None of the above eukaryotic DNA preparations could be amplified by the universal assay, thereby suggesting that this test is specific for bacteria. The ubiquity of the universal assay was verified by amplifying genomic DNAs from 116 reference strains which represent 95 of the most clinically relevant bacterial species. These species have been selected from the bacterial species listed in Tables 4 and 5. We found that 104 of these 116 strains could be amplified. The bacterial species which could not be amplified belong to the following genera: Corynebacterium (11 species) and Stenotrophomonas (1 species). Sequencing of the tuf genes from these bacterial species has been recently performed. This sequencing data has been used to select new universal primers which may be more ubiquitous. These primers are in the process of being tested. We also observed that for several species the annealing temperature had to be reduced to 45°C in order to get an efficient amplification. These bacterial species include Gemella morbilbrum, Listeria spp. (3 species) and Gardnerella vaginalis. It is important to note that the 95 bacterial species selected from Tables 4 and 5 to test the ubiquity of the universal assay include all of the most clinically relevant bacterial species associated with a variety of human infections acquired in the community or in hospitals (nosocomial infections). The most clinically important bacterial and fungal pathogens are listed in Tables 1 and 2.

10

15

20

30

35

EXAMPLES AND ANNEXES

The following examples and annexes are intended to be illustrative of the various methods and compounds of the invention, rather than limiting the scope thereof.

The various annexes show the strategies used for the selection of amplification primers from tuf sequences or from the recA gene: (i) Annex I illustrates the strategy used for the selection of the universal amplification primers from tuf sequences. (ii) Annex II shows the strategy used for the selection of the amplification primers specific for the genus Enterococcus from tuf sequences. (iii) Annex III illustrates the strategy used for the selection of the amplification primers specific for the genus Staphylococcus from tuf sequences. (iv) Annex IV shows the strategy used for the selection of the amplification primers specific for the species Candida albicans from tuf sequences. (v) Annex V illustrates the strategy used for the selection of the amplification primers specific for the genus Streptococcus from recA sequences. (vi) Annex VI gives a list of all selected primer pairs. As shown in these annexes, the selected amplification primers may contain inosines and/or degenerescences. Inosine is a nucleotide analog able to specifically bind to any of the four nucleotides A, C, G or T. Alternatively, degenerated oligonucleotides which consist of an oligonucleotide mix having two or more of the four nucleotides A, C, G or T at the site of mismatches were used. The inclusion of inosine and/or of degenerescences in the amplification primers allow mismatch tolerance thereby permitting the amplification of a wider array of target nucleotide sequences (Dieffenbach and Dveksler, 1995 PCR Primer; A Laboratory Manual, Cold Spring Harbor Laboratory Press, Plainview, New York).

EXAMPLES

25 **EXAMPLE 1**:

Selection of universal PCR primers from tuf sequences. As shown in Annex I, the comparison of tuf sequences from a variety of bacterial and eukaryotic species allowed the selection of PCR primers which are universal for the detection of bacteria. The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various tuf sequences. This multiple sequence alignment includes tuf sequences from 38 bacterial species and 3 eukaryotic species either determined by us or selected from databases (Table 13). A careful analysis of this multiple sequence alignment allowed the selection of primer sequences which are conserved within eubacteria but which discriminate sequences from eukaryotes, thereby permitting the universal detection of bacteria. As shown in Annex I, the selected primers contain several inosines and degenerescences. This was necessary because there is a relatively high polymorphism among bacterial tuf sequences despite the fact that this gene is highly conserved. In fact, among the tuf sequences that we determined, we found many nucleotide variations as well as some deletions and/or

10

15

20

25

30

35

insertions of amino acids. The selected universal primers were specific and ubiquitous for bacteria (Table 7). Of the 95 most clinically important bacterial species tested, 12 were not amplified. These species belong to the genera *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species). The universal primers did not amplify DNA of non-bacterial origin, including human and other types of eukaryotic DNA.

EXAMPLE 2:

Selection of genus-specific PCR primers from *tuf* sequences. As shown in Annexes 2 and 3, the comparison of *tuf* sequences from a variety of bacterial species allowed the selection of PCR primers specific for *Enterococcus* spp. or for *Staphylococcus* spp. The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various *tuf* sequences. These multiple sequence alignments include the *tuf* sequences of four representative bacterial species selected from each target genus as well as *tuf* sequences from species of other closely related bacterial genera. A careful analysis of those alignments allowed the selection of oligonucleotide sequences which are conserved within the target genus but which discriminate sequences from other closely related genera, thereby permitting the genus-specific and ubiquitous detection and identification of the target bacterial genus.

For the selection of primers specific for *Enterococcus* spp. (Annex II), we have sequenced a portion of approximately 890 bp of the *tuf* genes for *Enterococcus avium*, *E. faecalis*, *E. faecium* and *E. gallinarum*. All other *tuf* sequences used in the alignment were either sequenced by us or selected from databases. The analysis of this sequence alignment led to the selection of a primer pair specific and ubiquitous for *Enterococcus* spp. (Table 7). All of the 11 enterococcal species tested were efficiently amplified and there was no amplification with genomic DNA from bacterial species of other genera.

For the selection of primers specific for *Staphylococcus* spp. (Annex III), we have also sequenced a portion of approximately 890 bp of the *tuf* genes for *Staphylococcus aureus*, *S. epidermidis*, *S. saprophyticus* and *S. simulans*. All other *tuf* sequences used in the alignment were either sequenced by us or selected from databases. The analysis of this sequence alignment led to the selection of two primer pairs specific and ubiquitous for *Staphylococcus* spp. (Table 7). Annex III shows the strategy used to select one of these two PCR primer pairs. The same strategy was used to select the other primer pair. Of the 14 staphylococcal species tested, one (*S. sciuri*) could not be amplified by the *Staphylococcus*-specific PCR assays using either one of these two primer pairs, there was no amplification with DNA from species of other bacterial genera.

PCT/CA97/00829 -WO 98/20157

- 25 -

EXAMPLE 3:

5

10

15

20

25

30

35

Selection from tuf sequences of PCR primers specific for Candida albicans. As shown in Annex IV, the comparison of tuf sequences from a variety of bacterial and eukaryotic species allowed the selection of PCR primers specific for Candida albicans. The strategy used to design the PCR primers was based on the analysis of a multiple sequence alignment of various tuf sequences. This multiple sequence alignment includes tuf sequences of five representative fungal species selected from the genus Candida which were determined by our group (i.e. C. albicans, C. glabrata, C. krusei, C. parapsilosis and C. tropicalis) as well as tuf sequences from other closely related fungal species. tuf sequences from various bacterial species were also included. A careful analysis of this sequence alignment allowed the selection of primers from the C. albicans tuf sequence; these primers discriminate sequences from other closely related Candida species and other fungal species, thereby permitting the speciesspecific and ubiquitous detection and identification of C. albicans (Table 7). All of 88 Candida albicans strains tested were efficiently amplified and there was no amplification with genomic DNA from other fungal or bacterial species.

EXAMPLE 4:

Selection of PCR primers specific for Streptococcus from recA. As shown in Annex V, the comparison of the various bacterial recA gene sequences available from databases (GenBank and EMBL) was used as a basis for the selection of PCR primers which are specific and ubiquitous for the bacterial genus Streptococcus. Since sequences of the recA gene are available for many bacterial species including five species of streptococci, it was possible to choose sequences well conserved within the genus Streptococcus but distinct from the recA sequences for other bacterial genera. When there were mismatches between the recA gene sequences from the five Streptococcus species, an inosine residue was incorporated into the primer (Annex V). The selected primers, each containing one inosine and no degenerescence, were specific and ubiquitous for Streptococcus species (Table 7). This PCR assay amplified all of the 22 streptococcal species tested. However, the Streptococcus-specific assay did not amplify DNA from 3 out of 9 strains of S. mutans and 1 out of 3 strains of S. salivarius. There was no amplification with genomic DNA from other bacterial genera (Table 7).

EXAMPLE 5:

Nucleotide sequencing of DNA fragments. The nucleotide sequence of a portion of the tuf genes from a variety of bacterial or fungal species was determined by using the dideoxynucleotide chain termination sequencing method (Sanger et al., 1977, Proc. Natl. Acad. Sci. USA. 74:5463-5467). The sequencing was performed by using an Applied Biosystems automated DNA sequencer (model 373A) with their PRISM™ Sequenase® Terminator Double-stranded DNA Sequencing Kit (Perkin-Elmer Corp.,

10

15

20

25

30

35

Applied Biosystems Division, Foster City, CA). The sequencing strategy does not discriminate *tufA* and *tufB* genes because the sequencing primers hybridize efficiently to both bacterial *tuf* genes. These DNA sequences are shown in the sequence listing (SEQ ID Nos: 118 to 146). The presence of several degenerated nucleotides in the various *tuf* sequences determined by our group (Table 13) corresponds to sequence variations between *tufA* and *tufB*.

Oligonucleotide primers and probes selection. Oligonucleotide probes and amplification primers were selected from the given proprietary DNA fragments or database sequences using the Oligo™ program and were synthesized with an automated ABI DNA synthesizer (Model 391, Perkin-Elmer Corp., Applied Biosystems Division) using phosphoramidite chemistry.

EXAMPLE 6:

Labeling of oligonucleotides for hybridization assays. Each oligonucleotide was 5' end-labeled with $\gamma^{-32}P$ (dATP) by the T4 polynucleotide kinase (Pharmacia) as described earlier. The label could also be non-radioactive.

Specificity test for oligonucleotide probes. All labeled oligonucleotide probes were tested for their specificity by hybridization to DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6 as described earlier. Species-specific or genus-specific probes were those hybridizing only to DNA from the microbial species or genus from which it was isolated. Oligonucleotide probes found to be specific were submitted to ubiquity tests as follows.

Ubiquity test for oligonucleotide probes. Specific oligonucleotide probes were then used in ubiquity tests with strains of the target species or genus including reference strains and other strains obtained from various countries and which are representative of the diversity within each target species or genus. Chromosomal DNAs from the isolates were transferred onto nylon membranes and hybridized with labeled oligonucleotide probes as described for specificity tests. The batteries of isolates constructed for each target species or genus contain reference ATCC strains as well as a variety of clinical isolates obtained from various sources. Ubiquitous probes were those hybridizing to at least 80% of DNAs from the battery of clinical isolates of the target species or genus.

EXAMPLE 7:

Same as example 6 except that a pool of specific oligonucleotide probes is used for microbial identification (i) to increase sensitivity and assure 100% ubiquity or (ii) to identify simultaneously more than one microbial species and/or genus. Microbial identification could be performed from microbial cultures or directly from any clinical specimen.

10

15

20

30

35

EXAMPLE 8:

Same as example 6 except that bacteria or fungi were detected directly from clinical samples. Any biological sample was loaded directly onto a dot blot apparatus and cells were lysed *in situ* for bacterial or fungal detection and identification. Blood samples should be heparizined in order to avoid coagulation interfering with their convenient loading on a dot blot apparatus.

EXAMPLE 9:

PCR amplification. The technique of PCR was used to increase the sensitivity and the rapidity of the assays. The sets of primers were tested in PCR assays performed directly from bacterial colonies or from a standardized bacterial suspension (see Example 10) to determine their specificity and ubiquity (Table 7). Examples of specific and ubiquitous PCR primer pairs are listed in Annex VI.

Specificity and ubiquity tests for amplification primers. The specificity of all selected PCR primer pairs was tested against DNAs from a variety of bacterial and fungal species selected from Tables 4, 5 and 6 as described earlier. Primer pairs found specific for each species or genus were then tested for their ubiquity to ensure that each set of primers could amplify at least 90% of DNAs from a battery of isolates of the target species or genus. The batteries of isolates constructed for each species contain reference ATCC strains and various clinical isolates from around the world which are representative of the diversity within each species or genus.

Standard precautions to avoid false positive PCR results should be taken (Kwok and Higuchi, 1989, Nature, **239**:237-238). Methods to inactivate PCR amplification products such as the inactivation by uracil-N-glycosylase may be used to control PCR carryover.

25 **EXAMPLE 10**:

Amplification directly from bacterial or yeast cultures. PCR assays were performed either directly from a bacterial colony or from a bacterial suspension, the latter being adjusted to a standard McFarland 0.5 (corresponds to approximately 1.5 x 10^8 bacteria/mL). In the case of direct amplification from a colony, a portion of a colony was transferred using a plastic rod directly into a $20~\mu$ L PCR reaction mixture containing 50 mM KCl, 10 mM Tris-HCl (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl₂, 0.4 μ M of each primer, $200~\mu$ M of each of the four dNTPs and 0.5 unit of Taq DNA polymerase (Promega) combined with the TaqStartTM antibody (Clontech Laboratories Inc.). For the bacterial suspension, $1~\mu$ L of the cell suspension was added to $19~\mu$ L of the same PCR reaction mixture. For the identification from yeast cultures, $1~\mu$ L of a standard McFarland 1.0 (corresponds to approximately 3.0 x 10^8 bacteria/mL) concentrated 100 times by centrifugation was added directly to the PCR reaction. This concentration step for yeast cells was performed because a McFarland 0.5 for yeast cells has approximately 200 times fewer cells than a McFarland 0.5 for bacterial cells.

10

15

20

25

30

35

PCR reactions were then subjected to thermal cycling (3 min at 95°C followed by 30 cycles of 1 second at 95°C for the denaturation step and 30 seconds at 55°C for the annealing-extension step) using a PTC-200 thermal cycler. PCR amplification products were then analyzed by standard agarose gel (2%) electrophoresis. Amplification products were visualized in agarose gels containing 0.25 μ g/mL of ethidium bromide under UV at 254 nm. The entire PCR assay can be completed in approximately one hour.

Primer sequences derived from highly conserved regions of the bacterial 16S ribosomal RNA gene were used to provide an internal control for all PCR reactions. Alternatively, the internal control was derived from sequences not found in microorganisms or in the human genome. The internal control was integrated into all amplification reactions to verify the efficiency of the PCR assays and to ensure that significant PCR inhibition was absent. The internal control derived from rRNA was also useful to monitor the efficiency of the bacterial lysis protocols. The internal control and the species-specific or genus-specific amplifications were performed simultaneously in multiplex PCR assays.

EXAMPLE 11:

Amplification directly from urine specimens. For PCR amplification performed directly from urine specimens, 1 μ L of urine was mixed with 4 μ L of a lysis solution containing 500 mM KCl, 100 mM tris-HCl (pH 9.0), 1% triton X-100. After incubation for at least 15 minutes at room temperature, 1 μ L of the treated urine specimen was added directly to 19 μ L of the PCR reaction mixture. The final concentration of the PCR reagents was 50 mM KCl, 10 mM Tris (pH 9.0), 0.1% Triton X-100, 2.5 mM MgCl₂, 0.4 μ M of each primer, 200 μ M of each of the four dNTPs. In addition, each 20 μ L reaction contained 0.5 unit of Taq DNA polymerase (Promega) combined with the TaqStartTM antibody (Clontech Laboratories Inc.).

Strategies for the internal control, PCR amplification and agarose gel detection of the amplicons are as previously described in example 10.

EXAMPLE 12:

Detection of antibiotic resistance genes. The presence of specific antibiotic resistance genes which are frequently encountered and clinically relevant is identified using the PCR amplification or hybridization protocols described previously. Specific oligonucleotides used as a basis for the DNA-based tests are selected from the antibiotic resistance gene sequences. These tests, which allow the rapid evaluation of bacterial resistance to antimicrobial agents, can be performed either directly from clinical specimens, from a standardized bacterial suspension or from a bacterial colony and should complement diagnostic tests for the universal detection of bacteria as well as for the species-specific and genus-specific microbial detection and identification.

10

15

20

25

30

35

EXAMPLE 13:

Same as examples 10 and 11 except that assays were performed by multiplex PCR (i.e. using several pairs of primers in a single PCR reaction) to reach an ubiquity of 100% for the specific targeted pathogen(s). For more heterogeneous microbial species or genus, a combination of PCR primer pairs may be required to detect and identify all representatives of the target species or genus.

Multiplex PCR assays could also be used to (i) detect simultaneously several microbial species and/or genera or, alternatively, (ii) to simultaneously detect and identify bacterial and/or fungal pathogens and detect specific antibiotic resistance genes either directly from a clinical specimen or from bacterial cultures.

For these applications, amplicon detection methods should be adapted to differentiate the various amplicons produced. Standard agarose gel electrophoresis could be used because it discriminates the amplicons based on their sizes. Another useful strategy for this purpose would be detection using a variety of fluorescent dyes emitting at different wavelengths. The fluorescent dyes can be each coupled with a specific oligonucleotide linked to a fluorescence quencher which is degraded during amplification to release the fluorescent dyes (e.g. TaqManTM, Perkin Elmer).

EXAMPLE 14:

Detection of amplification products. The person skilled in the art will appreciate that alternatives other than standard agarose gel electrophoresis (Example 10) may be used for the revelation of amplification products. Such methods may be based on fluorescence polarization or on the detection of fluorescence after amplification (e.g. Amplisensor™, Biotronics; TaqMan™, Perkin-Elmer Corp.) or other labels such as biotin (SHARP Signal™ system, Digene Diagnostics). These methods are quantitative and may be automated. One of the amplification primers or an internal oligonucleotide probe specific to the amplicon(s) derived from the species-specific, genus-specific or universal DNA fragments is coupled with the fluorescent dyes or with any other label. Methods based on the detection of fluorescence are particularly suitable for diagnostic tests since they are rapid and flexible as fluorescent dyes emitting at different wavelengths are available.

EXAMPLE 15:

Species-specific, genus-specific, universal and antibiotic resistance gene amplification primers can be used in other rapid amplification procedures such as the ligase chain reaction (LCR), transcription-mediated amplification (TMA), self-sustained sequence replication (3SR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA), cycling probe technology (CPT) and branched DNA (bDNA) or any other methods to increase the sensitivity of the test. Amplifications can be performed from isolated bacterial cultures or directly from any clinical specimen. The scope of this invention is therefore not limited to the use of the

DNA sequences from the enclosed Sequence Listing for PCR only but rather includes the use of any procedures to specifically detect bacterial DNA and which may be used to increase rapidity and sensitivity of the tests.

EXAMPLE 16:

5

A test kit would contain sets of probes specific for each microbial species or genus as well as a set of universal probes. The kit is provided in the form of test components, consisting of the set of universal probes labeled with non-radioactive labels as well as labeled species- or genus-specific probes for the detection of each pathogen of interest in specific types of clinical samples. The kit will also include test reagents necessary to perform the pre-hybridization, hybridization, washing steps and hybrid detection. Finally, test components for the detection of known antibiotic resistance genes (or derivatives therefrom) will be included. Of course, the kit will include standard samples to be used as negative and positive controls for each hybridization test.

15

10

Components to be included in the kits will be adapted to each specimen type and to detect pathogens commonly encountered in that type of specimen. Reagents for the universal detection of bacteria will also be included. Based on the sites of infection, the following kits for the specific detection of pathogens may be developed:

20

- A kit for the universal detection of bacterial or fungal pathogens from all clinical specimens which contains sets of probes specific for highly conserved regions of the microbial genomes.

- A kit for the detection of microbial pathogens retrieved from urine samples, which contains 5 specific test components (sets of probes for the detection of *Enterococcus faecium, Enteroccus* species, *Staphylococcus* saprophyticus, *Staphylococcus* species and *Candida albicans*).

25

- A kit for the detection of respiratory pathogens which contains 3 specific test components (sets of probes for the detection of *Staphylococcus* species, *Enterococcus* species and *Candida albicans*).

30

- A kit for the detection of pathogens retrieved from blood samples, which contains 10 specific test components (sets of probes for the detection of Streptococcus species, Streptococcus agalactiae, Staphylococcus species, Staphylococcus saprophyticus, Enterococcus species, Enterococcus faecium, Neisseria species, Neisseria meningitidis, Listeria monocytogenes and Candida albicans). This kit can also be applied for direct detection and identification from blood cultures.

35

- A kit for the detection of pathogens causing meningitis, which contains 5 specific test components (sets of probes for the detection of *Streptococcus* species, *Listeria monocytogenes, Neisseria meningitidis, Neisseria* species and *Staphylococcus* species).

10

15

20

25

30

35

- A kit for the detection of clinically important antibiotic resistance genes which contains sets of probes for the specific detection of at least one of the 26 following genes associated with antibiotic resistance: bla_{tem} , bla_{rob} , bla_{shv} , bla_{oxa}

- Other kits adapted for the detection of pathogens from skin, abdominal wound or any other clinically relevant infections may also be developed.

EXAMPLE 17:

Same as example 16 except that the test kits contain all reagents and controls to perform DNA amplification assays. Diagnostic kits will be adapted for amplification by PCR (or other amplification methods) performed directly either from clinical specimens or from microbial cultures. Components required for (i) universal bacterial detection, (ii) species-specific and genus-specific bacterial and/or fungal detection and identification and (iii) detection of antibiotic resistance genes will be included.

Amplification assays could be performed either in tubes or in microtitration plates having multiple wells. For assays in plates, the wells will contain the specific amplification primers and control DNAs and the detection of amplification products will be automated. Reagents and amplification primers for universal bacterial detection will be included in kits for tests performed directly from clinical specimens. Components required for species-specific and genus-specific bacterial and/or fungal detection and identification as well as for the simultaneous antibiotic resistance genes detection will be included in kits for testing directly from bacterial or fungal cultures as well as in kits for testing directly from any type of clinical specimen.

The kits will be adapted for use with each type of specimen as described in example 16 for hybridization-based diagnostic kits.

EXAMPLE 18:

It is understood that the use of the probes and amplification primers described in this invention for bacterial and/or fungal detection and identification is not limited to clinical microbiology applications. In fact, we feel that other sectors could also benefit from these new technologies. For example, these tests could be used by industries for quality control of food, water, air, pharmaceutical products or other products requiring microbiological control. These tests could also be applied to detect and identify bacteria or fungi in biological samples from organisms other than humans (e.g. other primates, birds, plants, mammals, farm animals, livestock and others). These diagnostic tools could also be very useful for research purposes including clinical trials and epidemiological studies.

This invention has been described herein above, and it is readily apparent that modifications can be made thereto without departing from the spirit of this invention. These modifications are under the scope of this invention, as defined in the appended claims.

Table 1. Distribution (%) of nosocomial pathogens for various human infections in USA (1990-1992)¹.

	Pathogen	UTI ²	SSI ³	BSI⁴	Pneumonia	CSF⁵
5	Escherichia coli	27	9	5	4	2
	Staphylococcus aureus	2	21	17	21	2
	Staphylococcus epidermidis	2	6	20	0	1
	Enterococcus faecalis	16	12	9	2	0
	Enterococcus faecium	1	1	0	0	0
)	Pseudomonas aeruginosa	12	9	3	18	0
	Klebsiella pneumoniae	7	9 3 18 0 3 4 9 0 3 1 2 0 0 3 1 18 1 2 1 6 5 2 1 3 0 0 6 45	0		
	Proteus mirabilis	5	3	1	2	0
	Streptococcus pneumoniae	0	0	3	1	18
	Group B Streptococci	1	1	2	1	6
5	Other Streptococci	3	5	2	1	3
	Haemophilus influenzae	0	0	0	6	45
	Neisseria meningitidis	0	0	0	0	14
	Listeria monocytogenes	0	0	0	0	3
	Other Enterococci	1	1	0	0	0
)	Other Staphylococci	2		8	13	20
	Candida albicans	9	3	5	5	0
	Other Candida	2		1	3	10
	Enterobacter spp.	5	7	4	12	2
	Acinetobacter spp.	1	1	2	4	2
5	Citrobacter spp.	2	1	1	1	0
	Serratia marcescens	1	1	1	3	1
	Other Klebsiella	1	1	1	2	1
	Others	0	6	4	5	0

Data recorded by the National Nosocomial Infections Surveillance (NNIS) from 80 hospitals (Emori and Gaynes, 1993, Clin. Microbiol. Rev., **6**:428-442).

² Urinary tract infection.

³ Surgical site infection.

Bloodstream infection.

^{35 &}lt;sup>5</sup> Cerebrospinal fluid.

Table 2. Distribution (%) of bloodstream infection pathogens in Quebec (1995), Canada (1992), UK (1969-1988) and USA (1990-1992).

5	Organism	Quebec ¹	Canada ²	UK ³		USA⁴
				Community-	Hospital-	Hospital-
				acquired	acquired	acquired
	E. coli	15.6	53.8	24.8	20.3	5.0
	S. epidermidis	25.8	NI ⁶	0.5	7.2	31.0
	and other CoNS⁵					
10	S. aureus	9.6	NI	9.7	19.4	16.0
	S. pneumoniae	6.3	NI	22.5	2.2	NR ⁷
	E. faecalis	3.0	NI	1.0	4.2	NR
	E. faecium	2.6	NI	0.2	0.5	NR
	Enterococcus	NR	NI	NR	NR	9.0
15	spp.					
	H. influenzae	1.5	NR	3.4	0.4	NR
	P. aeruginosa	1.5	8.2	1.0	8.2	3.0
	K. pneumoniae	3.0	11.2	3.0	9.2	4.0
	P. mirabilis	NR	3.9	2.8	5.3	1.0
20	S. pyogenes	NR	NI	1.9	0.9	NR
	Enterobacter spp.	4.1	5.5	0.5	2.3	4.0
	Candida spp.	8.5	NI	NR	1.0	8.0
	Others	18.5	17.4 ⁸	28.7	18.9	19.0

- Data obtained for 270 isolates collected at the Centre Hospitalier de l'Université Laval (CHUL) during a 5 month period (May to October 1995).
 - ² Data from 10 hospitals throughout Canada representing 941 gram-negative bacterial isolates. (Chamberland *et al.*, 1992, Clin. Infect. Dis., **15**:615-628).
 - Data from a 20-year study (1969-1988) for nearly 4000 isolates (Eykyn *et al.*, 1990, J. Antimicrob. Chemother., Suppl. C, **25**:41-58).
 - Data recorded by the National Nosocomial Infections Surveillance (NNIS) from 80 hospitals (Emori and Gaynes, 1993, Clin. Microbiol. Rev., 6:428-442).
 - ⁵ Coagulase-negative staphylococci.

- ⁶ NI, not included. This survey included only gram-negative species.
- 35 ⁷ NR, incidence not reported for these species or genera.
 - 8 In this case, 17.4 stands for other gram-negative bacterial species.

Table 3. Distribution of positive and negative clinical specimens tested at the microbiology laboratory of the CHUL (February 1994 – January 1995).

5	Clinical specimens and/or sites	No. of samples tested (%)	% of positive specimens	% of negative specimens
	Urine	17,981 (54.5)	19.4	80.6
	Blood culture/marrow	10,010 (30.4)	6.9	93.1
	Sputum	1,266 (3.8)	68.4	31.6
	Superficial pus	1,136 (3.5)	72.3	27.7
10	Cerebrospinal fluid	553 (1.7)	1.0	99.0
	Synovial fluid	523 (1.6)	2.7	97.3
	Respiratory tract	502 (1.5)	56.6	43.4
	Deep pus	473 (1.4)	56.8	43.2
	Ears	289 (0.9)	47.1	52.9
15	Pleural and pericardial fluid	132 (0.4)	1.0	99.0
	Peritoneal fluid	101(0.3)	28.6	71.4
	Total:	32,966 (100.0)	20.0	80.0

Table 4. Gram-negative bacterial species (90) used to test the specificity of PCR primers and DNA probes (continues on next page).

	Bacterial species	Number of reference strains tested ^a	Bacterial species	Number of reference strains tested ^a
5	Acinetobacter baumannii	1	Moraxella phenylpyruvica	1
	Acinetobacter Iwoffii	3	Morganella morganii	1
	Actinobacillus lignieresii	1	Neisseria animalis	1
	Alcaligenes faecalis	1	Neisseria canis	1
	Alcaligenes odorans	1	Neisseria caviae	1
10	Alcaligenes xylosoxydans		Neisseria cinerea	1
	subsp. denitrificans	1	Neisseria cuniculi	1
	Bacteroides distasonis	1	Neisseria elongata subsp. elongata	1
	Bacteroides fragilis	1	Neisseria elongata subsp. glycoytica	1
	Bacteroides ovatus	1	Neisseria flavescens	1
15	Bacteroides	1	Neisseria flavescens	1
	thetaiotaomicron		Branham	
	Bacteroides vulgatus	1	Neisseria gonorrhoeae	18
	Bordetella bronchiseptica	1	Neisseria lactamica	1
	Bordetella parapertussis	1	Neisseria meningitidis	4
20	Bordetella pertussis	2	Neisseria mucosa	2
	Burkholderia cepacia	1	Neisseria polysaccharea	1
	Citrobacter amalonaticus	1	Neisseria sicca	3
	Citrobacter diversus subsp. koseri	2	Neisseria subflava	3
25	Citrobacter freundii	1	Neisseria weaveri	1
	Comamonas acidovorans	1	Ochrobactrum antropi	1
	Enterobacter aerogenes	1	Pasteurella aerogenes	1
	Enterobacter agglomerans	1	Pasteurella multocida	1
30	Enterobacter cloacae	1	Prevotella melaninogenica	1
	Escherichia coli	9	Proteus mirabilis	3
	Escherichia fergusonii	1	Proteus vulgaris	1

Bacterial species	Number of reference strains tested ^a	Bacterial species	Number of reference strains tested ^a
Escherichia hermannii	1	Providencia alcalifaciens	1
Escherichia vulneris	1	Providencia rettgeri	1
Flavobacterium meningosepticum	1	Providencia rustigianii	1
Flavobacterium indologenes	1	Providencia stuartii	1
Flavobacterium odoratum	1	Pseudomonas aeruginosa	14
Fusobacterium necrophorum	2	Pseudomonas fluorescens	2
Gardnerella vaginalis	1	Pseudomonas stutzeri	1
Haemophilus haemolyticus	1	Salmonella arizonae	1
Haemophilus influenzae	12	Salmonella choleraesuis	1
Haemophilus parahaemolyticus	1	Salmonella gallinarum	1
Haemophilus parainfluenzae	2	Salmonella typhimurium	3
Hafnia alvei	1	Serratia liquefaciens	1
Kingella indologenes subsp. suttonella	1	Serratia marcescens	1
Kingella kingae	1	Shewanella putida	1
Klebsiella ornithinolytica	1	Shigella boydii	1
Klebsiella oxytoca	1	Shigella dysenteriae	1
Klebsiella pneumoniae	8	Shigella flexneri	1
Moraxella atlantae	1	Shigella sonnei	1 🕙
Moraxella catarrhalis	5	Stenotrophomonas maltophilia	1
Moraxella lacunata	1	Yersinia enterocolitica	1
Moraxella osloensis	1		

Most reference strains were obtained from the American Type Culture Collection (ATCC). The other reference strains were obtained from (i) the Laboratoire de Santé Publique du Québec (LSPQ), (ii) the Center for Disease Control and Prevention (CDC) and (iii) the National Culture Type Collection (NCTC).

Table 5. Gram-positive bacterial species (97) used to test the specificity of PCR primers and DNA probes (continues on next page).

	Bacterial species	Number of	Bacterial species	Number of
		reference		reference
		strains		strains
		testedª		testedª
5	Abiotrophia adiacens	1	Micrococcus kristinae	1
	Abiotrophia defectiva	1	Micrococcus luteus	1
	Actinomyces israelii	1	Micrococcus lylae	1
	Clostridium perfringens	1	Micrococcus roseus	1.
	Corynebacterium accolens	1	Micrococcus varians	1
10	Corynebacterium aquaticum	1	Peptococcus niger	1
	Corynebacterium bovis	1	Peptostreptococcus anaerobius	1
	Corynebacterium cervicis	1	Peptostreptococcus	1 4
		0	asaccharolyticus	40
15	Corynebacterium diphteriae	6	Staphylococcus aureus	10
	Corynebacterium flavescens	1	Staphylococcus auricularis	1
	Corynebacterium	6	Staphylococcus capitis	1
	genitalium		subsp. <i>urealyticus</i>	
20	Corynebacterium jeikeium	1	Staphylococcus cohnii	1
	Corynebacterium kutcheri	1	Staphylococcus epidermidis	2
	Corynebacterium	1	Staphylococcus	2
	matruchotii		haemolyticus	
	Corynebacterium	1	Staphylococcus hominis	2
25	minutissimum			
	Corynebacterium	1	Staphylococcus	1
	mycetoides		lugdunensis	
	Corynebacterium	1	Staphylococcus	3
	pseudodiphtheriticum		saprophyticus	
30	Corynebacterium	6	Staphylococcus schleiferi	1
	pseudogenitalium			
	Corynebacterium renale	1	Staphylococcus sciuri	1
	Corynebacterium striatum	1	Staphylococcus simulans	1
	Corynebacterium ulcerans	11	Staphylococcus warneri	11

Bacterial species	Number of	Bacterial species	Number of
	reference		reference
	strains		strains
	testeda		test e dª
Corynebacterium	1	Staphylococcus xylosus	1
urealyticum			
Corynebacterium xerosis	1	Streptococcus agalactiae	6
Enterococcus avium	1	Streptococcus anginosus	2
Enterococcus	1	Streptococcus bovis	2
casseliflavus			
Enterococcus cecorum	1	Streptococcus constellatus	1
Enterococcus dispar	1	Streptococcus crista	1
Enterococcus durans	1	Streptococcus dysgalactiae	1
Enterococcus faecalis	6	Streptococcus equi	1
Enterococcus faecium	3	Streptococcus gordonii	1
Enterococcus flavescens	1	Group C Streptococci	1
Enterococcus gallinarum	3	Group D Streptococci	1
Enterococcus hirae	1	Group E Streptococci	1
Enterococcus mundtii	1	Group F Streptococci	1
Enterococcus	1	Group G Streptococci	1
pseudoavium			
Enterococcus raffinosus	1	Streptococcus intermedius	1
Enterococcus	1	Streptococcus mitis	2
saccharolyticus		•	
Enterococcus solitarius	1	Streptococcus mutans	1
Eubacterium lentum	1	Streptococcus oralis	1
Gemella haemolysans	1	Streptococcus parasanguis	1
Gemella morbillorum	1	Streptococcus pneumoniae	6
Lactobacillus acidophilus	1	Streptococcus pyogenes	3
Listeria innocua	1	Streptococcus salivarius	2
Listeria ivanovii	1	Streptococcus sanguis	2
Listeria grayi	1	Streptococcus sobrinus	1
Listeria monocytogenes	3	Streptococcus suis	1
Listeria murrayi	1	Streptococcus uberis	1
Listeria seeligeri	1	Streptococcus vestibularis	1
Listeria welshimeri	1	•	

Most reference strains were obtained from the American Type Culture Collection
 (ATCC). The other reference strains were obtained from (i) the Laboratoire de Santé Publique du Québec (LSPQ), (ii) the Center for Disease Control and Prevention (CDC) and (iii) the National Culture Type Collection (NCTC).

Table 6. Fungal species (12) used to test the specificity of PCR primers and DNA probes.

Fungal species	Number of reference strains tested ^a
Candida albicans	12
Candida glabrata	1
Candida guilliermondii	1
Candida kefyr	3
Candida krusei	2
Candida lusitaniae	1
Candida parapsilosis	2
Candida tropicalis	3
Rhodotorula glutinis	1
Rhodotorula minuta	1
Rhodotorula rubra	1
Saccharomyces cerevisiae	1

Most reference strains were obtained from (i) the American Type Culture Collection
 (ATCC) and (ii) the Laboratoire de Santé Publique du Québec (LSPQ).

Table 7. PCR assays developed for several clinically important bacterial and fungal pathogens (continues on next page).

	Organism	Primer Pair ^a	Amplicon	Ubiquity ^b	DNA amp	lification from
		SEQ ID NO	size (bp)		culture	specimens⁴
	Enterococcus faecium	1-2	216	79/80	+	+
5	Listeria monocytogenes	3-4	130	164/168°	+	+
	Neisseria meningitidis	5-6	177	258/258	+	+
	Staphylococcus saprophyticus	7-8	149	245/260	+	NT
10	Streptococcus agalactiae	9-10	154	29/29	+	+
	Candida albicans	11-12	149	88/88	+	NT
	Enterococcus	13-14	112	87/87	+	NT
	spp. (11 species) ^f					
	Neisseria spp.	15-16	103	321/321	+	+
15	(12 species) ^f					
	Staphylococcus spp.	17-18	192	13/14	+	NT
	(14 species)					
	. •	19-20	221	13/14	+	NT
	Streptococcus spp.	21-22	153	210/214 ⁹	+	+
20	(22 species) ^f					
	Universal detection ^h	23-24	309	104/ 116 ⁱ	+	+
	(95 species) ⁱ					

- a All primer pairs are specific in PCR assays since no amplification was observed with DNA from the bacterial and fungal species other than the species of interest listed in Tables 4, 5 and 6.
 - b Ubiquity was tested by using reference strains as well as strains from throughout the world, which are representatite of the diversity within each target species or genus.
- ^c For all primer pairs, PCR amplifications performed directly from a standardized microbial suspension (MacFarland) or from a colony were all specific and ubiquitous.
 - d PCR assays performed directly from blood cultures, urine specimens or

- cerebrospinal fluid. NT, not tested.
- The four *L. monocytogenes* strains undetected are not clinical isolates. These strains were isolated from food and are not associated with a human infection.
- The bacterial species tested include all those clinically relevant for each genus (Tables 4 and 5). All of these species were efficiently amplified by their respective genus-specific PCR assay, except for the *Staphylococcus*-specific assay, which does not amplify *S. sciuri*.
 - The Streptococcus-specific PCR assay did not amplify 3 out of 9 strains of S. mutans and 1 out of 3 strains of S. salivarius.
- 10 h The primers selected for universal bacterial detection do not amplify DNA of non-bacterial origin, including human and other types of eukaryotic genomic DNA.
 - For the universal amplification, the 95 bacterial species tested represent the most clinically important bacterial species listed in Tables 4 and 5. The 12 strains not amplified are representatives of genera *Corynebacterium* (11 species) and *Stenotrophomonas* (1 species).

Table 8. Target genes for the various genus-specific, species-specific and universal amplification assays.

Microorganisms	Gene	Protein encoded
Candida albicans	tuf	translation elongation factor EF-Tu
Enterococcus faecium	ddl	D-alanine:D-alanine ligase
Listeria monocytogenes	actA	actin-assembly inducing protein
Neisseria meningitidis	omp	outer membrane protein
Streptococcus agalactiae	cAMP	cAMP factor
Staphylococcus saprophyticus	unknown	unknown
Enterococcus spp.	tuf	translation elongation factor EF-Tu
Neisseria spp.	asd	ASA-dehydrogenase
Staphylococcus spp.	tuf	translation elongation factor EF-Tu
Streptococcus spp.	<i>rec</i> A	RecA protein
Universal detection	tuf	translation elongation factor EF-Tu

Table 9. Antibiotic resistance genes selected for diagnostic purposes.

	Genes	Genes SEQ ID NOs		Antibiotics	Bacteria ^a
	-	selected primers	originating fragment	-	
5	bla _{oxa}	49-50	110	β-lactams	Enterobacteriaceae, Pseudomonadaceae
	blaZ	51-52	111	β-lactams	Enterococcus spp.
	aac6'-lla	61-64	112	Aminoglycosides	Pseudomonadaceae
	ermA	91-92	113	Macrolides	Staphylococcus spp.
10	ermB	93-94	114	Macrolides	Staphylococcus spp.
	ermC	95-96	115	Macrolides	Staphylococcus spp.
	vanB	71-74	116	Vancomycin	Enterococcus spp.
	vanC	75-76	117	Vancomycin	Enterococcus spp.
	aad(6')	173-174	_	Streptomycin	Enterococcus spp.

^a Bacteria having high incidence for the specified antibiotic resistance genes. The presence of these antibiotic resistance genes in other bacteria is not excluded.

Table 10. Antibiotic resistance genes from our co-pending US (N.S. 08/526840) and PCT (PCT/CA/95/00528) patent applications for which we have selected PCR primer pairs.

5	Genes	SEQ ID NOs	Antibiotics	Bacteriaª
		of selected primers		
	bla _{tem}	37-40	β-lactams	Enterobacteriaceae,
				Pseudomonadaceae,
				Haemophilus spp.,
				Neisseria spp.
	blarob	45-48	β-lactams	Haemophilus spp.,
				Pasteurella spp.
10	blashv	41-44	β-lactams	Klebsiella spp.
				and other
				Enterobacteriaceae
	aadB	53-54	Aminoglycosides	Enterobacteriaceae,
	aacC1	55-56		Pseudomonadaceae
	aacC2	57-58		
15	aacC3	59-60		
	aacA4	65-66		
	mecA	97-98	β-lactams	Staphylococcus spp.
	<i>van</i> A	67-70	Vancomycin	Enterococcus spp.
	satA	81-82	Macrolides	Enterococcus spp.
20	aac(6')-aph(2")	83-86	Aminoglycosides	Enterococcus spp.,
				Staphylococcus spp.
	vat	87-88	Macrolides	Staphylococcus spp.
	vga	89-90	Macrolides	Staphylococcus spp.
	msrA	77-80	Erythromycin	Staphylococcus spp.
	int	99-102	β-lactams,	Enterobacteriaceae,
25			trimethoprim,	
	sul	103-106	aminoglycosides,	Pseudomonadaceae
			antiseptic,	
			chloramphenicol	

^a Bacteria having high incidence for the specified antibiotic resistance genes. The presence of these antibiotic resistance genes in other bacteria is not excluded.

Table 11. Correlation between disk diffusion and PCR amplification of antibiotic resistance genes in *Staphylococcus* species^a.

				Disk d	iffusion (Kirby-B	auer) ^b
5	Antibiotic	Phenotype	PCR	Resistant	Intermediate	Sensitive
	Penicillin	blaZ	+	165	0	0
			-	0	0	31
	Oxacillin	mecA	+	51	11	4
			-	2	0	128
10	Gentamycin	aac(6')aph(2'')	+	24	18	6
			-	0	0	148
	Erythromycin	ermA	+	15	0	0
		ermB	+	0	0	0
		ermC	+	43	0	0
15		msrA	+	4	0	0
			-	0	1	136

- ^a The Staphylococcus strains studied include S. aureus (82 strains), S. epidermidis (83 strains), S. hominis (2 strains), S. capitis (3 strains), S. haemolyticus (9 strains), S. simulans (12 strains) and S. warneri (5 strains), for a total of 196 strains.
- Susceptibility testing was performed by the method of Kirby-Bauer according to the protocol reccommended by the National Committee of Clinical Laboratory Standards (NCCLS).

Table 12. Correlation between disk diffusion profiles and PCR amplification of antibiotic resistance genes in *Enterococcus* species^a.

		_	Disk diffusion	on (Kirby-Bauer) ^b	
Antibiotic	Phenotype	PCR	Resistant	Sensitive	
	blaZ	+	0	2	
Ampicillin					
		-	1	30	
Gentamycin	aac(6')aph(2")	+	51	1	
		=	3	38	
Streptomycin	<i>aad</i> (6')	+	26	15	
		-	6	27	
Vancomycin	vanA	+	36	0	
	vanB	+	26	0	
		-	0	40	

^a The *Enterococcus* strains studied include *E. faecalis* (33 strains) and *E. faecium* (69 strains), for a total of 102 strains.

Susceptibility testing was performed by the method of Kirby-Bauer according to the protocol reccommended by the National Committee of Clinical Laboratory Standards (NCCLS).

Table 13. Origin of *tuf* sequences in the Sequence Listing (continues on next page).

	SEQ ID NO	Bacterial or fungal species	Source
5	118	Abiotrophia adiacens	This patent
	119	Abiotrophia defectiva	This patent
	120	Candida albicans	This patent
	121	Candida glabrata	This patent
	122	Candida krusei	This patent
10	123	Candida parapsilosis	This patent
	124	Candida tropicalis	This patent
	125	Corynebacterium accolens	This patent
	126	Corynebacterium diphteriae	This patent
	127	Corynebacterium genitalium	This patent
15	128	Corynebacterium jeikeium	This patent
	129	Corynebacterium	This patent
		pseudotuberculosis	
	130	Corynebacterium striatum	This patent
	131	Enterococcus avium	This patent
	132	Enterococcus faecalis	This patent
20	133	Enterococcus faecium	This patent
	134	Enterococcus gallinarum	This patent
	135	Gardnerella vaginalis	This patent
	136	Listeria innocua	This patent
	137	Listeria ivanovii	This patent
25	138	Listeria monocytogenes	This patent
	139	Listeria seeligeri	This patent
	140	Staphylococcus aureus	This patent
	141	Staphylococcus epidermidis	This patent
	142	Staphylococcus saprophyticus	This patent
30	143	Staphylococcus simulans	This patent
	144	Streptococcus agalactiae	This patent
	145	Streptococcus pneumoniae	This patent

	SEQ ID NO	Bacterial or fungal species	Source
	146	Streptococcus salivarius	This patent
	147	Agrobacterium tumefaciens	Database
	148	Bacillus subtilis	Database
	149	Bacteroides fragilis	Database
5	150	Borrelia burgdorferi	Database
	151	Brevibacterium linens	Database
	152	Burkholderia cepacia	Database
	153	Chlamydia trachomatis	Database
	154	Escherichia coli	Database
10	155	Fibrobacter succinogenes	Database
	156	Flavobacterium ferrugineum	Database
	157	Haemophilus influenzae	Database
	158	Helicobacter pylori	Database
	159	Micrococcus luteus	Database
15	160	Mycobacterium tuberculosis	Database
	161	Mycoplasma genitalium	Database
	162	Neisseria gonorrhoeae	Database
	163	Rickettsia prowazekii	Database
	164	Salmonella typhimurium	Database
20	165	Shewanella putida	Database
	166	Stigmatella aurantiaca	Database
	167	Streptococcus pyogenes	Database
	168	Thiobacillus cuprinus	Database
	169	Treponema pallidum	Database
25	170	Ureaplasma urealyticum	Database
	171	Wolinella succinogenes	Database
		·	

Corynebacterium CCACCGTTAC CGGTATCGAG ATGTTCC...AGATGGT CATGCCTGGC GACAACGTCG

trachomatis

diphteriae

	Annex I:	Strategy for the selection from tuf sequences of the universal amplification	a
		primers (continues on pages 49 to 51).	
		ŎES	E C
		491 517776 802 N	N S
Ŋ	Abiotrophia	CAACTGTAAC TGGTGTTGAA ATGTTCCAAATGGT AATGCCTGGT GATAACGTAA	118
	adiacens		
	Abiotrophia	CTACCGTTAC CGGTGTTGAA ATGTTCCAAATGGT TATGCCAGGC GACAACGTAC	119
	defectiva		
	Agrobacterium	CGACTGTTAC CGGCGTTGAA ATGTICCAAAIGGI TATGCCTGGC GACAACGICA	147
10	tumefaciens		
	Bacillus	CA <u>ACTGITAC AGGIGIIGAA AIGII</u> CCAA <u>AIGGI TAIGCCIGGA GAIAACA</u> CTG	148
	subtilis)
	Bacteroides	CAGT <u>IGIAAC AGGIGIIGAA AIGII</u> CCAA <u>AIGGI AAIGCCGGGI GATAACGI</u> AA	149
	fragilis		.
15	Borrelia	CT <u>actgitac iggigitigaa aigti</u> ccaa <u>aiggi iaigcciggi gataaig</u> itg	150
	burgdorferi		
	Brevibacterium	CGACTGICAC CGCIAICGAG AIGIICCAGAIGGI CAIGCCCGGC GACACCACCG	151
	linens		
	Burkholderia	CGACCIGCAC GGGCGTIGAA AIGIICCAAAIGGI CAIGCCGGGC GACAACGIGT	152
20	cepacia		
	Chlamydia	CGATIGITAC IGGGGTIGAA AIGIICAAGAIGGI CAIGCCIGGG GAIAACGIIG	153

	Mycoplasma	CAGTIGITAC IGGAAITGAA AIGIICAAAAIGGI ICIACCIGGI GAIAAIGCIT	161
	genitalium		
	Neisseria	CCACCTGTAC CGGCGTTGAA ATGTTCCAAATGGT AATGCCGGGT GAGAACGTAA	162
	gonorrhoeae		
Ŋ	Rickettsia	CGACTIGIAC AGGIGIAGAA AIGTICAAGAIGGI IAIGCCIGGA GATAAIGCTA	163
	prowazekii		
	Salmonella	CT <u>acctgtac tggcgttgaa atgtt</u> ccag <u>atggt</u>	164
	${ t typhimurium}$		
	Shewanella	CA <u>acgigtac iggigtagaa aigti</u> ccag <u>aiggi aaigccaggc gataacai</u> ca	165
10	putida		
	Stigmatella	CGGT <u>CAICAC GGGGGTGGAG AIGTI</u> CCAG <u>AIGGI GAIGCCGGGA GACAACAI</u> CG	166
	aurantiaca		
	Staphylococcus	CA <u>ACTGTTAC AGGTGTTGAA ATGTT</u> CCAA <u>ATGGT AATGCCTGGT GATAACGT</u> TG	140
	aureus		
15	Staphylococcus	CAACTGITAC TGGIGIAGAA AIGIICCAAAIGGI TAIGCCIGGC GACAACGIIG	141
	epidermidis		
	Streptococcus	CA GT<u>IGTTAC</u> IGGIGIIGAA AIGII CCAAAI GGI TAIGCCIGGI GATAACGI TA	144
	agalactiae		
	Streptococcus	CAGT <u>IGITAC IGGIGIIGAA AIGII</u> CCAA <u>AIGGI AAIGCCIGGI GAIAACGI</u> GA	145
20	pneumoniae		
	Streptococcus	CTGT <u>TGTTAC TGGTGTTGAA ATGTT</u> CCAAATGG <u>T TATGCCTGGT GATAACGT</u> GA	167
	pyogenes		
	${\it Thiobacillus}$	CCACCTGCAC CGGCGTGGAA ATGTTCAAAATGGT CATGCCCGGC GATAATGT	168
	cuprinus		
25	Treponema	CAGTGGTTAC TGGCATTGAG ATGTTTAACATGGT GAAGCCGGGG GATAACACCA	169
	pallidum		

	Ureaplasma	lasma	CTGTIGITAC AGGAAITGAA AIGITTAATTIGGI TAIGCCAGGI GAIGACGI	170
	urealy	urealyticum		
	Wolinella	9 <i>11a</i>	CA <u>accgtaac iggcgttgag atgtt</u> ccag <u>atggt tatgcctggt gacaacgt</u> ta	171
	succir	succinogenes		
'n	Candida	la	GTGT <u>T</u> AC <u>CAC <u>TGAAGTC</u>AAR TCCG<u>T</u>TGAGRAAT<u>T GGAAGAAAAT</u> CC<u>AAA</u>AT<u>T</u>CG</u>	120
	albicans	sus		
	Schizo-	(GTGT <u>CACTAC CGAAGTCAAG</u> TCTG <u>T</u> TGAG <u>AAGAT TGAGGAG</u> TC <u>C</u> CC <u>TAA</u> GT <u>T</u> TG	
	saccha	saccharomyces pombe	отре	
	Human		TG <u>acaggca</u> t <u>tgagatg</u> ttc cacaagaag <u>aaggag</u> c <u>t</u> tg <u>cc</u> atg cc <u>c</u> ggggagg	
10	Selectedª	;edª	ACIKKIAC IGGIGTIGAR ATGTT ATGGT IATGCCIGGI GALAAYRT	
	equencesª	es ^a		
	Selected	,ed	SEQ ID NO: 23	
	universal	:sal		
15	primer	ζ,	ACIKKIAC IGGIGTIGAR ATGTT AYRTT ITCICCIGGC ATIACCAT	
	sequences*:	ıcesª:		
	Ę			
	THE SE	adnence num	ine sequence numbering relets to the b. coil tur gene tragment. Underlined nucleotides are	
	identi	cal to the	identical to the selected sequence or match that sequence.	
20	rs	"I" stands	"I" stands for inosine which is a nucleotide analog that can bind to any of the four	
		nucleotides A,	es A, C, G or T. "K", "R" and "Y" designate nucleotide positions which are	
		degenerated.	ed. "K" stands for T or G; "R" stands for A or G; "Y" stands for C or T.	
	д	This sequence	ence is the reverse complement of the above tuf sequence.	

for		SEQ	-
ers specific		435	
for the selection from tuf sequences of the amplification primers specific for	ad 54).		
ences o	es 53 a	401	
on from tuf seque	Enterococcus (continues on pages 53 and 54).	348	
for the selection			
Strategy	the genus	314	
Annex II:			

5 Bacillus	cgcga c<u>actg</u> <u>aaaaaccatt</u> <u>caigaig</u>cca gttgacgcgg acaa<u>gtiaaa gicggigacg aagti</u>gaaat	ID NO 148
subtilis Bacteroides	CGCGA <u>IGTIG ATAAACCTIT</u> <u>CTIGAIG</u> CCG GTAGAACTGG TGTTA <u>ICCAT GTAGGIGATG AAAI</u> CGAAAT	149
fragilis Burkholderia	cgtgc agt<u>tg Ac</u>ggcg<u>cgtt</u> <u>cc<u>tgatg</u>ccg gtggacgcgg catc<u>gt</u>gaag <u>gtcggcgaag aaat</u>cgaaat</u>	152
10 cepacia Chlamydia	AGAGA A<u>ATIG ACAAGCCTIT</u> <u>CTIAAIG</u>CCT ATTGACGTGG AATT<u>GTIAAA GTT</u>TCC<u>GA</u>TA <u>AAGTT</u>CAGTT	153
trachomatis Corynebacterium	CGTGA <u>GACCG ACAAGCCATT CCTCATG</u> CCT ATCGACGTGG CTCC <u>CTGAAG GT</u> CAAC <u>GAGG ACGT</u> CGAGAT	126
diphteriae 15 <u>Enterococcus</u>	CGTGA <u>TACTG ACAAACCATT</u> <u>CATGATG</u> CCA GTCGACGTGG ACAA <u>GTTCGC</u> <u>GTTGGTGACG AAGTT</u> GAAAT	131
<u>avium</u> Enterococcus faecalis	CGTGA tactg acaaaccait catgaig cca gtcgacgtgg tgaa gticgc gttggtgacg aagti gaaat	132

	134		154	
	.CGTGG ACAA <u>GTTCGC GTTGGTGA</u> T <u>G AAGT</u> AGAAAT		.CGCGG TATCA <u>rcaaa Gttggtgaag aagtt</u> gaaat	
	CGTGA <u>tactg acaaaccatt catgatg</u> cca gtcgacgtgg acaa <u>gticgc gttggtga</u> t <u>g aagt</u> agaaat		CGTGCGAT <u>IG ACAAGCCGGII CCIGCIG</u> CCG ATCGACGCGG TATCA <u>ICAAA GTIGGIGAAG AAGIT</u> GAAAT	
20 <u>faecium</u>	Enterococcus	gallinarum	Escherichia	coli

CGTGACAACG ACAAACCAIT CAIGAIGCCA GITGA...CGTGG ACAAGIICGC GITGGIGACG AAGIIGGAAGI

Enterococcus

Gardnerella	CACGA <u>ICTIG acaagccati</u> <u>Ct<u>igatg</u>cca atcgacgtgg taagc<u>icc</u>ca a<u>i</u>caacac<u>c</u>c <u>cagti</u>gagat</u>	135
vaginalis		
Haemophilus	CGTGCGATIG ACCAACCGTI CCITCITCCA ATCGACGAGG TATTAICCGT ACAGGIGAIG AAGTAGAAAT	157
influenzae		
5 Helicobacter	agaga c<u>actg aaaaaacttt</u> ct<u>tgatg</u>ccg gttgaagagg cgtg<u>gtgaaa gtaggcga</u>tg <u>aagt</u>ggaaat	158
pylori		
Listeria	CGTGA <u>tactg acaaaccatt catgatg</u> cca gttgacgtgg acaa <u>gttaaa gttggtgacg aagta</u> gaagt	138
monocytogenes		
Micrococcus	CGCGAC <u>AAGG ACAAGCCGTT CCIGATG</u> CCG ATCGACGCGG CACCC <u>IGAAG AICAACTCCG AGGI</u> CGAGAT	159
10 luteus		
Mycobacterium	CGCGAG <u>acce acaagccgtt cctgatg</u> ccg gtcgacgcgg cgtga <u>tcaac gtgaacgagg aagtt</u> gagat	160
tuberculosis		
Mycoplasma	cgtga agta<u>g ataaaccttt</u> ctiatia gca attgaagagg tgaac <u>icaaa gtaggicaag aagti</u> gaaat	161
genitalium		
15 Neisseria	CGTGC CGTG<u>G ACAAACCATT</u> <u>CCIGCIG</u>CCT ATCGACGAGG TATC<u>AICCAC GTTGGIGACG AGAII</u>GAAAT	162
gonorrhoeae		
Salmonella	CGTGCGAT <u>IG ACAAGCCGTI CCIGCIG</u> CCG ATCGACGCGG TATCA <u>ICAAA GIGGGCGAAG AAGTI</u> GAAAT	164
typhimurium		
Shewanella	CGTGACATC <u>G ATAAGCCGTT CCTACTG</u> CCA ATCGACGTGG TATT <u>GTACGC GTAGGCGACG AAGTT</u> GAAAT	165
20 putida		
Staphy l ococcus	CGTGA <u>ITCIG ACAAACCATI</u> CAIGAIGCCA GTTGACGTGG TCAAA <u>ICAAA GTTGGTGAAG AAGTI</u> GAAAT	140
aureus		
Staphy l ococcus	CGTGA <u>ITCIG ACAAACCAIT CAIGAIG</u> CCA GTTGACGTGG TCAAA <u>ICAAA GIWGGTGAAG AAGTI</u> GAAAT	141
epidermidis		
25 Staphylococcus	CGTGA <u>ITCIG ACAAACCAII CAIGAIG</u> CCA GTTGACGTGG TCAAA <u>ICAAA GICGGTGAAG AAAIC</u> GARAT	142
saprophyticus		

Streptococcus	CGTGATACTG ACAAACCTTT	ac <u>t</u> rc <u>r</u> tcca	GTTGAC	GTGG 1	ACTGTTCGT	<u>ACAAACCTIT</u> AC <u>ITCI</u> TCCA GTTGACGTGG TACT <u>GITCG</u> T <u>GTCAACGACG AAGIT</u> GAAAT	GAAAT	144
agalactiae								
Streptococcus	CGTGACACTG ACAAACCATT	GCTTCTTCCA	GTCGAC	GTGG 1	ATCGTTAAA	<u>acaaaccait</u> gc <u>itci</u> tcca gtcgacgtgg tatc <u>gtiaaa gicaacgacg aa</u> aicgaaat	GAAAT	145
pneumoniae								
5 Streptococcus	CGCGACACTG ACAAACCATT	GCITCII	GTCGAC	GTGG 1	ACTGTTCGT	<u>acaaaccatt</u> gc <u>itci</u> tcca gtcgacgtgg tact <u>giicg</u> t <u>gicaacgacg aaat</u> cgaaat	GAAAT	167
pyogenes								
${\it Ureaplasma}$	CGTAGIACIG ACAAACCAII	CTTATTAGCA	ATTGAC	GTGG 1	GTATTAAAA	<u>acaaaccatt cttatta</u> gca attgacgtgg tgtat <u>taaaa gttaatga</u> t <u>g aggtt</u> gaaat	GAAAT	170
urealyticum								
Selected	TACTG ACAAACCATT	CATGATG			GTICGC	GTTGGTGACG AAGTT	F.1	
10 sednences								

SEQ ID NO: 14ª		AACTIC GICACCAACG CGAAC	
SEQ ID NO: 13		TACTG ACAAACCATT CATGATG	
Selected	genus-specific	primer	15 sequences:

The sequence numbering refers to the E. faecalis tuf gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence

This sequence is the reverse complement of the above tuf sequence. 20

The above primers also amplify tuf sequences from Abiotrophia species; this genus has recently been related to the Enterococcus genus by 168 rRNA analysis. NOTE:

for the selection from tuf sequences of the amplification primers specific for	us (continues on pages 56 and 57).
Strategy for the selection	the genus Staphylococcus (
nnex III:	

Annex III:	Strategy for the selection from tuf sequences of the amplification primers	s specific for	
	the genus Staphylococcus (continues on pages 56 and 57).		
	385	611 SEQ ID	Д
		NO	
5 Bacillus	TGG <u>CCGTGT</u> A <u>GAACGCGGAC AAGTTAAA</u> GT CGGTTG CTAAA <u>CCAGG TACAATCAC</u> T	CCACACAGCA 148	
subtilis			
Bacteroides	AGGT <u>CGTAT</u> C <u>GAA</u> AC <u>TGGI</u> G TTATCCATGT AGGTTT GTAAA <u>CCGGG T</u> CAG <u>ATTAAA CCTCAC</u> TCTA	CTCACTCTA 149	
fragilis			
Burkholderia	GGGT <u>CGTGT</u> C <u>GAGCGCG</u> CA TCG <u>TGAA</u> GGT CGGTGG CGAAG <u>CCGGG TTCGATCAC</u> G	<u>ccgcaca</u> cgc 152	
10 cepacia			
${\it Chlamydia}$	TGGA <u>CGTATT GAGCGTGG</u> AA TTG <u>TTAAA</u> GT TTCTTT GCTTG <u>CC</u> AAA <u>CAGTGTTAAA</u>	CCTCATACAC 153	
trachomatis			
Corynebacterium	m CGG <u>CCGTGTT GAGCGTGG</u> CT CCCTGAAGGT CAATTG TTAAG <u>CCAGG GGCTTACAC</u> C <u>CCTCACA</u> CCG	CTCACA	
diphteriae			
15 Enterococcus	AGGACGIGII GAACGIGGIG AAGIICGCGI IGGIAG CIAAACCAGC IACAAICACI	CCACACA	
faecalis			
Enterococcus	AGGT <u>CGTGTT GAACGTGGAC AAGT</u> TCGCGT TGGTAG CTAAA <u>CCAGG TACAATCACA</u>	<u>cctcrta</u> caa 133	
faecium			
Escherichia	CGGT <u>CGTGT</u> A <u>GAACGCGGT</u> A TC <u>ATCAAA</u> GT TGGTGG CTAAG <u>CCGGG CACCATCA</u> AG	CCGCACA	
20 coli			
Gardnerella	CGGT <u>CGTGTT GAGCGTGGTA AGCTC</u> CCAAT CAATGG CT <u>GCTCCAGG TTCTGTGAC</u> T <u>CCACACA</u> CCA	CACACACCA 135	
vaginalis			

Haemophilus	AGGT <u>CGTGT</u> A GAACGAGGTA TTATCCGTAC AGGTAG CGAAA <u>CCAGG TTCAATCACA CCACACA</u> CTG 157
influenzae	
${\it Helicobacter}$	AGG TA<u>GGAIT GAAAGAGG</u>CG TGG<u>IGAAA</u>GT AGGTAT GCAAA<u>CCAGG ITCTATCAC</u>T <u>CCGCACA</u>AGA 158
pylori	
5 Listeria	TGGA <u>CGTGTT GAACGTGGAC AAGTTAAA</u> GT TGGTAG CTAAA <u>CCAGG TTCGATTAC</u> T <u>CCACACA</u> CTA 138
monocytogenes	
Micrococcus	CGGT <u>CGCGCC GAGCGCGG</u> CA CCC <u>IGAA</u> GAT CAATGG TG <u>GAGCCGGG CTCCATCAC</u> C <u>CCGCACA</u> CCA 159
luteus	
Mycobacterium	CGGA <u>CGTGT</u> G GAG <u>CGCGG</u> CG TG <u>ATCAA</u> CGT GAATCA CCAAG <u>CCCGG CACCACCG CCGCACACA</u> CCG
10 tuberculosis	
Mycoplasma	AGG AA<u>GAGTT GAAAGAGGT</u>G <u>AACTCAAA</u>GT AGGTAG CAAAA<u>CCAGG CTCTATTAAA CCGCACA</u>AGA 161
genitalium	
Neisseria	CGG <u>CCGIGIA GAGCGAGGI</u> A TC <u>AICCA</u> CGT IGGTGG CCAAA <u>CGGGG IACTAICAC</u> T <u>CCTCACA</u> CCA 162
gonorrhoeae	
15 Salmonella	CGGT <u>CGTGT</u> A <u>GAGCGCGGT</u> A TC <u>ATCAAA</u> GT GGGTGG CTAAG <u>CCGGGG CACCATCAAG CCGCACA</u> CCA 164
typhimurium	
Shewanella	AGGT <u>CGTGTT GAGCGTGGT</u> A TTG <u>T</u> ACGCGT AGGTAG CGAAG <u>CCAGG TTCAATCA</u> AC <u>CCACACA</u> CTA 165
putida	
Staphylococcus	AGG <u>CCGTGTT GAACGTGGTC AAATCAAA</u> GT TGGTAG CT <u>GCTCCTGG TTCAATTACA CCACATA</u> CTG 140
20 <u>aureus</u>	
Staphylococcus	AGG <u>CCGTGTT GAACGTGGTC AAATCAAA</u> GT WGGTAG CT <u>GCTCCTGG TTCTATTACA CCACACA</u> CAA 141
epidermidis	
Staphylococcus	AGG <u>CCGIGIT GAACGIGGIC AAAICAAA</u> GI CGGIAG CI <u>GCICCIGG IACTAICACA CCACAIA</u> CAA 142
saprophyticus	
25 Staphylococcus	AGG <u>CCGTGTT GAACGTGGTC AAATCAAA</u> GT CGGTAG CA <u>GCTCCTGG CTCTATTACT CCACACA</u> CAA 143
simulans	

TRIGIGGI GIRAIWGWRC CAGGAGC

CCGTGTT GAACGTGGTC AAATCAAA

genus-specific

sequences:

primer

ACACTA 144		:ACACTA 145		ACCGTA 170		AYA		
CTAAACCAGG TTCAATCAAC CCAC		CTAAACCAGG TTCAATCAAC CCAC		TAAAACCAGG A <u>TCAATTAAA CC</u> TC		GCTCCTGG YWCWATYACA CCACAYA		SEO ID NO: 18 ^b
AGGA <u>CGIAI</u> C <u>GA</u> CC <u>GIGGIA</u> CTGITCGIGT CAATTG CTAAA <u>CCAGG TTCAAICA</u> AC <u>CCACACA</u> CTA		AGGACGIAIC GACCGIGGIA TCGITAAAGT CAATCG CTAAACCAGG ITCAATCAAC CCACACACTA		GAACGIGGIG TATIAAAAGT TAATTG TAAAACCAGG AICAATTAAA CCTCACCTA		CCGIGIT GAACGIGGIC AAAICAAA		SEO ID NO: 17
AGGACGTATC		AGGA <u>CGTAT</u> C		TGGACGTGTT		CCGTGT		
Streptococcus	agalactiae	Streptococcus	pneumoniae	5 Ureaplasma	urealyticum	Selected	sednences	0.00 co.00 c

15 The sequence numbering refers to the S.aureus tuf gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

"R", "W" and "Y" designate nucleotide positions which are degenerated. "R" stands for A or G; "W", for A or T; "Y", for C or T.

This sequence is the reverse complement of the above tuf sequence.

Strategy for the selection from tuf sequences of the amplification primers specific for the species Candida albicans (continues on pages 59 and 60). Annex IV:

ON CI	120		121		122		123		124					153		126		132		154	
213 SEQ	GITGGITACA ACCCAAAGAC TGTCAA AICCGGIAAA GITACIGGIA AGACCITGTT		ACCCAAAGAC IGTCAA GGCTGGTGTC GICAAGGGIA AGAYCITGTT		TGTCAA GGCAGGTGTT GTTAAGGGTA AGACCTTATT		GIIGGIIACA ACCCIAAAGC TGITAA AGCIGGIAAG GIIACCGGIA AGACCIIGIT		TGTCAA GGCTGGTAAG GTTACCGGTA AGACTTTGTT		ACCCCAAGAC CGTCAA GGCTGGTGTC GICAAGGGIA AGACTCTTTT		CTAGTT AGGCCTGAAG TCIGTGCAGA AGCTACTGGA	<u>AI</u> G <u>IA</u> T <u>I</u> CTGG <u>AG</u> CTGATGAA		CTGAGCAGGA TTAGAA GTGGACCCAG TCCATCATCG ACCTCATGCA		T <u>gaagaa</u> aaa <u>a</u> tcttag <u>a</u> attaatggc		GGGAAGCG AAAATCCTGG AACTGGCTGG	
181	CAA		CAA		CAA		TAA		CAA		CAA		GTT	CTTCAA		GAA		:		:	
90	C TGT.		c rgr.				c rgr.				c car.		G CTA.			A TTA.		A TTT.		A CTT.	
	CAAAGA		CAAAGA		GTTGGTTACA ACCCAAAGAC		<u>CTAA</u> AG		ACCCTAAGGC		CCAAGA		CCGAGTTTGG	<u>GCaagta</u> cgg		AGCAGG		GACTTAITAT CAGAATACGA TTT.		CTCAGTACGA CTT	
	ACA ACC				ACA ACC		ACA ACC		ACA ACC									rat cac		rer crg	
	FTGGTT		GICGGITACA		TIGGTT?		regett?		GTTGGTTACA		GICGGTITCA		<u>G</u> AGCTGCT <u>CA</u>	GAGCTGCTCA		GAGCTGCTCG		ACTTAI		GAACTICTGT	
	BAAG G						SAAG G						<u>10</u> <u>0</u> 500					rcer g			
58	CGT <u>CAAGAAG</u>		CATCAAGAAG		CATCAAGAAG		CGTCAAGAAG		CGT <u>CAAGAAG</u>		CATCAAGAAG		GGAGATCCGG	GGAGCTGCGC		GGAGATCCRT		GGAAGTTCGT		GGAAGTTCGT	
												pombe				mn					
	Candida	albicans	Candida	glabrata	Candida	krusei	Candida	parapsilosis	10 Candida	tropicalis	Schizo-	saccharomyces pombe	Human	15 Chlamydia	trachomatis	Corynebacterium	diphteriae	Enterococcus	faecalis	Escherichia	coli
				ស					10					15					20		

	Flavobacterium	CGAGGTICGC GAAGAACTGA CTAAACGCGG TTTGGGT <u>TAAA GAAATIGAAA A</u> CCTGATGGA	156
	ferrugineum		
	Gardnerella	AGAGGTCCGT GACCTCCTCG AAGAAAACGG CTTCAA GIGGGTAGAG ACCGTCAAGG AACTCATGAA	135
	vaginalis		
Ŋ	5 Haemophilus	GGAAGTICGI GAACT <u>I</u> CTAI CI <u>CAA</u> IATGA CITGG <u>G</u> AAG <u>AA</u> AAA <u>A</u> TCCT <u>IG AG</u> TIAGCAAA	157
	influenzae		
	Listeria	gga <u>aa</u> tt cgt <u>gai</u>cta<u>t</u>ta<u>a</u> ctga<u>ata</u>tga attgg<u>g</u>aagct aaa<u>atig</u>acg <u>ag</u>ttaatgga	138
	monocytogenes		
	Micrococcus	GGAAGTCCGT GAGTTGCTGG CTGCCCAGGA ATTCAA GIGGGTCGAG TCIGTCACAC AGTTGATGGA	159
10	10 luteus		
	Neisseria	GGAAATCCGC GACCTGCTGT CCAGCTACGA CTTACGAAGAA AAAATCTTCG AACTGGCTAC	162
	gonorrhoeae		
	Salmonella	GGAAGTICGC GAACTGCTGT CTCAGTACGA CTTGGGAAGCG AAAATCATCG AACTGGCTGG	164
	typhimurium		
15	15 Staphylococcus	ggaagticgi gactta <u>i</u> ta <u>a</u> gcga <u>a</u> t <u>a</u> tga cit <u>cg</u> aa <u>gaa</u> aaa <u>a</u> icttag <u>a</u> attaatgga	140
	aureus		
	Streptococcus	GGAAATCCGT GACCTAITGT CAGAATACGA CTT <u>CG</u> AAGAC AICGTIATGG AATTGATGAA	145
	pneumoniae		
	Treponema	AGAGGIGCGI GAIGCGCIIG CIGGAIAIGG GITGGA GGAIGCAGCI IGIAIIGAGG AACIGCITGC	169
20	20 pallidum		

Selected	CAAGAAG GTTGGTTACA ACCCAAAGA	ATCCGGTAAA GTTACTGGTA AGACCT
Selected	SEQ ID NO: 11	SEQ ID NO: 12ª
5 species-specific		
primer	CAAGAAG GTTGGTTACA ACCCAAAGA	AGGICTTACC AGTAACTITAC CGGAI
sednences:		

10 The sequence numbering refers to the Candida albicans tuf gene fragment. Underlined nucleotides are identical to the selected sequence or match that sequence.

This sequence is the reverse-complement of the above tuf sequence.

	Annex V:	Strategy for	ny for the	selection from the recA gene of	n from	the re	acA ger		the amplification primers	icatic	n primer	s specific	fic for	
		the ger	the genus Streptococcus (continues on pages) snooooo	contin	nes on	pages	62 and	63).					
		415	75				449.	449540					574 SEQ	Q
													ON CI	0
5	5 Bordetella	5	CTC <u>GAGAT</u> CA	CCGACGCGCI	I GGIG	CGCICG	GGCTC.	GGCC	GGIGCGCTCG GGCTCGGCCC GCCIGAIGAG CCAGGCGCTG	SAG CC	AGGCGCTG	CGCAAGCTGA	CTGA	
	pertussis													
	Burkholderia	ឡ	CTCGAAAICA CCGAIGCGCI	CCGATGCGC	I GGIG	CGCTCG	GGCTC.	6600	GGIGCGCTCG GGCTCGGCCC GCCIGAIGTC GCAGGCGCIG	gra a <u>c</u>	<u>AGGCGCTG</u>	CGCAAGCTGA	CTGA	
	cepacia													
	Campylobacter	LJ	TTA <u>gaaattg</u> t <u>agaaa</u> cta <u>t</u> agcaagaagt ggcgcagcaa gac <u>ttaig</u> tc <u>tcaagc</u> tc <u>ta agaaa</u> actta	T <u>AGAAA</u> CTA	I AGCA	AGAAGT	GGCGC	AGCA	A GAC <u>TTATC</u>	TC IC	AAGCTCTA	AGAAAA	CTTA	
10	10 jejuni													
	Chlamydia	I	TTGAGTATTG	CAGAGCTCII AGCGCGTTCT GGAGCAGCTC GCATGAIGTC GCAGGCTCIA CGCAAATTAA	I AGCG	CGTTCT	GGAGC	AGCT	C GCATGAT	grc G	AGGCTCIA	CGCAAA	TTAA	
	trachomatis													
	${\it Clostridium}$	I	TTA <u>GAAAT</u> AA	CAGAAGCTII AGIIAGATCA GGAGCAGCTA GATIAAIGTC ACAAGCCTIA AGAAAGTTAA	I AGII	AGATCA	GGAGC	AGCT	A GAT <u>TAAT</u>	grc Ag	AAGCCTIA	aga <u>aa</u> g	TTAA	
	perfringens													
15	15 Corynebacterium		CTG <u>GAGATTG</u>	CAGAIATGCI TGIICGCTCT GGAGCAGCGC GTTIGAIGAG	T TGTT	CGCTCT	GGAGC	AGCG	C GTT <u>TGAT</u>		TCAGGCGCTG	CGTAA GATGA	ATGA	
	pseudotuberculosis	osis												
	Enterobacter	ຍ	CTGGAAATCT	GTGAIGCGCI GACCCGTTCA GGCGCAGCTC GTAIGAIGAG CCAGGCGAIG	T GACC	CGTTCA	25255	AGCT	C GTATGAT	GAG CC	AGGCGATG	CGTAAGCTTG	CTTG	
	agglomerans													
	Enterococcus	T	TTA <u>GAGATTG</u>	CCGAIGCCIT AGIITCAAGT GGTGCAGCTC GACIAAIGTC ICAAGCACTA CGIAAA	T AGII	TCAAGT	GGTGC	AGCT	c GAC <u>IAAI</u> C	grc IC	AAGCACTA	CGTAAA	TTAT	
20	faecium													
	Escherichia	ស	CTG <u>GAAAT</u> CT	GTGACGCCCI		CGTTCT	၁၅၁၅၅	GGCA	GGCGCGTTCT GGCGCGGCAC GTATGATGAG		CCAGGCGATG	CGTAAGCTGG	CTGG	
	, Lon													

GCGA <u>acagaa gaataggaatt</u> ttaatgcatt accgcgacct gtga <u>gttta</u> c <u>gcaaagcttg</u> agac <u>a</u> ttaaa	TTA <u>gaaat</u> t t <u>agaaa</u> cga <u>t</u> c <u>a</u> ccagaagc ggaggagcaa ggc <u>itaigag</u> c <u>catgcgtta agaaa</u> aatca		CTTC <u>aaattg CtGaaaaatt gatt</u> acttct ggagcagcac gt <u>atgatg</u> tc a <u>caagccatg cgtaa</u> acttg		CTG <u>gaaatta Ctgala</u> tgc <u>t gglg</u> cgttct gcagcggcaa gat <u>tgatg</u> tc <u>gcaagcctig cgtaa</u> attga		TIT GCTC<u>tt</u>a tc<u>gaa</u>tc<u>att</u> a<u>attaa</u>aaca aacaatgcaa ga<u>atgatg</u>tc aa<u>aag</u>gtt<u>tg</u> <u>cgaa</u>gaatac		TTG <u>gaaaict gcgaca</u> cgc <u>t</u> cg <u>i</u> ccgttcg ggcggggcgc gcc <u>tgatgag icaggc</u> tt <u>ig cgcaa</u> actga		CTG <u>gaaatt</u> t gtgaigcatt atc<u>i</u>cg ctct ggtgccgcac gt <u>atgatgag ccaagctatg</u> <u>cgtaa</u> actag		CTG <u>gaaat</u> ca <u>ccgaca</u> tgc <u>t</u> ggigcg ctcc aacgcggcac gcc <u>igaig</u> tc c <u>caggcgctg cgcaa</u> gatca		CTG <u>gaaat</u> ct gtgaigcgc <u>t</u> <u>gaccc</u> gctcc ggcgcggcgc gc <u>atgaigag</u> c <u>caggcgaig</u> <u>cgtaa</u> gctgg		CTG <u>GAAAICT GTGACGCCCT</u> GGCGCGTTCT GGCGCGGCAC GT <u>ATGATGAG CCAGGCGATG CGTAA</u> GCTGG		15 CTT <u>GAAATCG CCGAAGCATT</u> TG <u>TTAG</u> AAGT GGTGCAGCTC GT <u>TAATG</u> TC A <u>CAAGCGTTA CGTAA</u> ACTTT		TIAGAAAIIG CAGGAAAAII GAIIGACTCT GGGGC		E CIT <u>GAAAIIG CAGGGAAAII GAIIGA</u> IICI GGCGCAGCAC GC <u>AIGAIGAG ICAAGCGAIG CGIAA</u> AITAI 3	
Haemophilus	influenzae Helicobacter	pylori	5 Lactococcus	lactis	Legionella	pneumophila	Mycoplasma	10 genitalium	Neisseria	gonorrhoeae	Proteus	mirabilis	15 Pseudomonas	aeruginosa	Serratia	marcescens	Shigella	20 flexneri	Staphy l o c oc c u s	aureus	Streptococcus	gordonii	25 Streptococcus	mit and

G CCAGGCCATG CGTAAACTTG 34		G TCAGGCCATG CGTAAATTAT 35		G TCAAGCCATG CGTAAACTTT 36		c ccaaccaate cctaa		G CCAGGCTAIG CGIAAGCTGG		ATGAIGAG TCAIGCCAIG CGTAA		SEQ ID NO: 22b		TTACGCAT GGCITGACTC ATCAT	
GGCTC GT <u>ATGATGA</u>		AGCAC GTATGATGA		AGCGC GT <u>ATGATGA</u>		AGCGC GT <u>ATGTTG</u> T		cecec gr <u>argaiga</u>		ATGATGA				TTACGCA	
CTTGAGATIG CGGGAAAAII GATIGACTCA GGTGCGGCTC GTAIGAIGAG CCAGGCCAIG CGIAAACTTG		CTTGAAATTG CAGGIAAATT GATTGATTCT GGTGCAGCAC GTATGATGAG TCAGGCCATG CGIAAATTAT		CIC <u>GAAATIG CAGGIAAGCI GAIIGA</u> CICI GGIGCAGCGC GI <u>AIGAIGAG ICAAGCCAIG CGIAA</u> ACTIT		CIG <u>gaaatt</u> t gigaigc <u>act</u> ggcicgctct ggtgcagcgc gtaigtigtc g <u>caagcaatg cgtaa</u> actga		CTGGAAATIT GTGAIGCGCI GACICGCTCT GGTGCCGCGC GTAIGAIGAG CCAGGCTAIG		GAAATIG CAGGIAAATI GAITGA		SEQ ID NO: 21		GAAATTG CAGGIAAATT GATTGA	
Streptococcus	pneumoniae	Streptococcus	pyogenes	5 Streptococcus	salivarius	Vibrio	cholerae	Yersinia	10 pestis	Selected	sednences	Selected	15 genus-specific	primer	sednencesª:

"I" stands for inosine which is a nucleotide analog that can bind to any of the four nucleotides to the selected sequence or match that sequence. 20

The sequence numbering refers to the S.pneumoniae recA sequence. Underlined nucleotides are identical

G or T. ບັ Ъ, ф

This sequence is the reverse complement of the above recA sequence.

Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ II	NO Nucleotide sequence	Originating	DNA fragment
			SEQ ID	Nucleotide
			NO	position
_	<u>Bacter</u>	rial species: Enterococcus faecium		
5				
	1	5'-TGC TTT AGC AAC AGC CTA TCA G	26ª	273-294
	2 ^b	5'-TAA ACT TCT TCC GGC ACT TCG	26ª	468-488
	Bacter	tial species: Listeria monocytogenes		
10				
	3	5'-TGC GGC TAT AAA TGA AGA GGC	27ª	339-359
	4 ^b	5'-ATC CGA TGA TGC TAT GGC TTT	27ª	448-468
15	Bacter	ial species: Neisseria meningitidis		
.0	5	5'-CCA GCG GTA TTG TTT GGT GGT	28ª	56-76
	6 _p	5'-CAG GCG GCC TTT AAT AAT TTC	28ª	212-232
20	<u>Bacter</u>	ial species: Staphylococcus saprophyt	icus	
20	7	5'- AGA TCG AAT TCC ACA TGA AGG TTA T	TA TGA 29°	290-319
	8 _p	5'- TCG CTT CTC CCT CAA CAA TCA AAC T	AT CCT 29°	409-438
25	Bacter	ial species: Streptococcus agalactiae		
	9	5'-TTT CAC CAG CTG TAT TAG AAG TA	30ª	59-81
	10 ^b	5'-GTT CCC TGA ACA TTA TCT TTG AT	30ª	190-212
30	<u>Fungal</u>	species: Candida albicans		
	1.1	5'-CAA GAA GGT TGG TTA CAA CCC AAA GA	. 120°	61-86
	12 ^b	5'-AGG TCT TAC CAG TAA CTT TAC CGG AT	120°	184-209

^a Sequences from databases.

³⁵ b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

^c Sequences determined by our group.

Annex VI: Specific and ubiquitous primers for DNA amplification (continues on next page)

•	····										 	
	SEQ ID	NO N	ucle	otid	le se	quen	.ce				Originating	DNA fragment
											SEQ ID	Nucleotide
											NO	position
5	Bacter	ial genu	1S:	Ente	rocc	occus	•					
	13	5 ' - TA C	TGA	CAA	ACC	ATT	CAT	GAT	G		131-134 ^{a,b}	319-340°
	14 ^d	5'-AAC	TTC	GTC	ACC	AAC	GCG	AAC			131-134 ^{a,b}	410-430°
	Bacter	ial genu	ıs:	Neis	seri	a	4					
10												
	15	5'-CTG									31 ^e	21-40 ^f
	16 ^d	5'-GCC	GAC	GTT	GGA	AGT	GGT	AAA	G		31 ^e	102-123 ^f
	Bacter:	ial genu	<u>15:</u>	Stap	hylo	coco	us					
15	17	5'-CCG	TGT	TGA	ACG	TGG	TCA	AAT	CAA	A	140-143 ^{a,b}	391-415 ^g
	18ª	5'-TRT	GTG	GTG	TRA	TWG	WRC	CAG	GAG	С	140-143 ^{a,b}	58 4- 608 ⁹
	19	5'-ACA	ACG	TGG	WCA	AGT	\mathtt{WTT}	AGC	WGC	Т	140-143 ^{a,b}	562-583 ^g
	20 ^d	5'-ACC	ATT	TCW	GTA	CCT	TCT	GGT	AAG	T	140-143 ^{a,b}	729-753 ^g
20	Bacteri	ial genu	1 s :	Stre	ptoc	coccu	ıs					
	21	5'-GAA	ATT	GCA	GGI	AAA	TTG	ATT	GA		32-36°	418-440 ^h
	22 ^d	5'-TTA	CGC	ATG	GCI	TGA	CTC	ATC	AT		32-36 ^e	547-569 ^h
25				Univ	versa	al pi	cime	cs				
	23	5'-ACI	KKI	ACI	GGI	GTI	GAR	ARG	TT		118-146 ^{a,b}	493-515 ⁱ
											147-171 ^{a,e}	
	24 ^d	5'-AYR	TTI	TCI	CCI	GGC	ITA	ACC	AT		118-146 ^{a,b}	778-800 ⁱ
											147-171 ^{a,e}	

- 30 a These sequences were aligned to derive the corresponding primer.
 - b tuf sequences determined by our group.
 - $^{\rm c}$ The nucleotide positions refer to the E. faecalis tuf gene fragment (SEQ ID NO: 132).
- These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.
 - Sequences from databases.
 - $^{
 m f}$ The nucleotide positions refer to the N. meningitidis asd gene fragment (SEQ ID NO: 31).

- $^{\rm g}$ The nucleotide positions refer to the S. aureus tuf gene fragment (SEQ ID NO: 140).
- ^h The nucleotide positions refer to the S. pneumoniae recA gene (SEQ ID NO: 34).
- 5 i The nucleotide positions refer to the $E.\ coli\ tuf$ gene fragment (SEQ ID NO: 154).

Annex VI: Specific and ubiquitous primers for DNA amplification

	SEQ II	NO Nucleotide sequence	Originating	DNA fragment
			SEQ ID	Nucleotide
			NO	position
_	<u>Antibi</u>	otic resistance gene: bla _{tem}		
5	37	5'-CTA TGT GGC GCG GTA TTA TC	-	-
	38	5'-CGC AGT GTT ATC ACT CAT GG	-	-
	39	5'-CTG AAT GAA GCC ATA CCA AA	-	-
10	40	5'-ATC AGC AAT AAA CCA GCC AG	-	-
	<u> Antibi</u>	otic resistance gene: blashv		
	41	5'-TTA CCA TGA GCG ATA ACA GC	_	. <u>-</u>
4-	42	5'-CTC ATT CAG TTC CGT TTC CC	-	-
15	43	5'-CAG CTG CTG CAG TGG ATG GT		_
	44	5'-CGC TCT GCT TTG TTA TTC GG	-	-
	Antibi	lotic resistance gene: blarob		
20	<u> </u>	TOD		
	45	5'-TAC GCC AAC ATC GTG GAA AG	-	-
	46	5'-TTG AAT TTG GCT TCT TCG GT	-	-
	47	5'-GGG ATA CAG AAA CGG GAC AT	-	-
25	48	5'-TAA ATC TTT TTC AGG CAG CG		~-
	Antibi	totic resistance gene: blaoxa		
	49	5'-GAT GGT TTG AAG GGT TTA TTA TAA G	110ª	686-710
30	50 ^b	5'-AAT TTA GTG TGT TTA GAA TGG TGA T	110ª	802-826
	Antibi	lotic resistance gene: blaz		
	51	5'-ACT TCA ACA CCT GCT GCT TTC	111ª	511-531
35	52 ^b	5'-TGA CCA CTT TTA TCA GCA ACC	111ª	663-683
	<u>Antibi</u>	iotic resistance gene: aadB		
	53	5'-GGC AAT AGT TGA AAT GCT CG	-	-
40	54	5'-CAG CTG TTA CAA CGG ACT GG	-	-
	<u>Antibi</u>	iotic resistance gene: aacC1		
	55	5'-TCT ATG ATC TCG CAG TCT CC	_	
45	56	5'-ATC GTC ACC GTA ATC TGC TT		-

^a Sequences from databases.

SUBSTITUTE SHEET (RULE 26)

b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

Annex VI: Specific and ubiquitous primers for DNA amplification

SEQ I	D NO Nucleotide sequence	Originating	DNA fragme
		SEQ ID	Nucleotide
		NO	position
Antib	iotic resistance gene: aacC2		
57	5'-CAT TCT CGA TTG CTT TGC TA	-	
58	5'-CCG AAA TGC TTC TCA AGA TA	-	-
Antib	iotic resistance gene: aacC3		
59	5'-CTG GAT TAT GGC TAC GGA GT		-
60	5'-AGC AGT GTG ATG GTA TCC AG	-	-
<u>Antib</u>	iotic resistance gene: aac6'-IIa		
61	5'-GAC TCT TGA TGA AGT GCT GG	112ª	123-1
62 ^b	5'-CTG GTC TAT TCC TCG CAC TC	112ª	284-3
63 64 ^b	5'-TAT GAG AAG GCA GGA TTC GT 5'-GCT TTC TCT CGA AGG CTT GT	112ª 112ª	445-4 522-5
-			
<u>Antib</u>	iotic resistance gene: aacA4		
65	5'-GAG TTG CTG TTC AAT GAT CC	-	-
66	5'-GTG TTT GAA CCA TGT ACA CG	-	-
<u>Antib</u>	iotic resistance gene: aad(6')		
173	5'-TCT TTA GCA GAA CAG GAT GAA	_	-
174	5'-GAA TAA TTC ATA TCC TCC G	-	-
<u>Antib</u>	iotic resistance gene: vanA		
67	5'-TGT AGA GGT CTA GCC CGT GT	-	-
68	5'-ACG GGG ATA ACG ACT GTA TG		-
69	5'-ATA AAG ATG ATA GGC CGG TG	-	_
70	5'-TGC TGT CAT ATT GTC TTG CC	-	-
<u>Antib</u>	iotic resistance gene: vanB		
71	5'-ATT ATC TTC GGC GGT TGC TC	116ª	22-41
72 ^b	5'-GAC TAT CGG CTT CCC ATT CC	116ª	171-1
73	5'-CGA TAG AAG CAG CAG GAC AA	116ª	575-5
74 ^b	5'-CTG ATG GAT GCG GAA GAT AC	116ª	713-7

a Sequences from databases.

SUBSTITUTE SHEET (RULE 26)

^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

Annex VI: Specific and ubiquitous primers for DNA amplification

SEQ :	ID NO Nucleotide sequence	Originati	ng DNA fragmen
		SEQ ID	Nucleotide
		NO	position
Antil	oiotic resistance gene: vanC		
75	5'-GCC TTA TGT ATG AAC AAA TGG	117ª	373-39
76 ^b	5'-GTG ACT TTW GTG ATC CCT TTT GA	117ª	541-56
Antil	piotic resistance gene: msrA		
77	5'-TCC AAT CAT TGC ACA AAA TC	-	_
78	5'-AAT TCC CTC TAT TTG GTG GT	-	-
79	5'-TCC CAA GCC AGT AAA GCT AA	-	-
80	5'-TGG TTT TTC AAC TTC TTC CA	-	-
Antil	piotic resistance gene: satA		
81	5'-TCA TAG AAT GGA TGG CTC AA	-	-
82	5'-AGC TAC TAT TGC ACC ATC CC	-	-
Antil	piotic resistance gene: aac(6')-aph	(2")	
83	5'-CAA TAA GGG CAT ACC AAA AAT C	-	-
84	5'-CCT TAA CAT TTG TGG CAT TAT C		-
85	5'-TTG GGA AGA TGA AGT TTT TAG A	-	-
86	5'-CCT TTA CTC CAA TAA TTT GGC T	-	-
Antil	piotic resistance gene: vat		
87	5'-TTT CAT CTA TTC AGG ATG GG	-	~
88	5'-GGA GCA ACA TTC TTT GTG AC	~	-
Antil	oiotic resistance gene: vga		
89	5'-TGT GCC TGA AGA AGG TAT TG	-	-
90	5'-CGT GTT ACT TCA CCA CCA CT	-	-
Antil	piotic resistance gene: ermA		
91	5'-TAT CTT ATC GTT GAG AAG GGA TT	113ª	370-39
91			

⁴⁵ a Sequences from databases.

b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

Annex VI: Specific and ubiquitous primers for DNA amplification

SEQ :	ID NO	NO Nucleotide sequence						Originating DNA				
											fragmen	ıt
											SEQ	Nucleotide
											ID NO	position
Anti	biotic	resi	.sta	nce	gene	<u>2</u> : 6	ermB					
93	5'-	CTA I	rct	GAT	TGT	TGA	AGA	AGG	ATT		114ª	366-389
94 ^b	5 ' -	GTT I	rac	TCT	TGG	TTT	AGG	ATG	AAA		114ª	484-507
<u>Antil</u>	biotic	resi	sta	nce	gene	: e z	mC					
95	5!-	CTT G	TT	GAT	CAC	GAT	דעע	TTC	۲		115ª	214-235
96 ^b		ATC I							_		115ª	382-403
Antil	biotic	resi	sta	nce	gene	: n	ecA					
	· · · · · ·											
97		AAC A									-	-
98	5'-	ATT G	CT	GTT	AAT	ATT	TTT	TGA	GTT	GAA	-	-
Antil	biotic	resi	sta	nce	gene	<u>:</u> : i	nt					
99	5'-	GTG A	ATC	GAA	ATC	CAG	ATC	С			-	_
100	5'-	ATC C	CTC	GGT	TTT	CTG	GAA	G			-	-
101	5'-	CTG G	TC.	ATA	CAT	GTG	ATG	G			_	
102	5 ' -	GAT G	TT.	ACC	CGA	GAG	CTT	G			-	-
<u>Antil</u>	biotic	resi	.sta:	nce	gene	<u>:</u> .s	ul					
103	5'-	TTA A	AGC	GTG	CAT	AAT	AAG	CC			-	_
104	5'-	TTG C	CGA	TTA	CTT	CGC	CAA	CT			-	-
105	5' -	TTT A	ACT .	AAG	CTT	GCC	CCT	TC			_	-
106	5'-	AAA A	AGG	CAG	CAA	TTA	TGA	GC			-	

³⁵ a Sequences from databases.

^b These sequences are from the opposite DNA strand of the sequence of the originating fragment given in the Sequence Listing.

- 71 -

SEOUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT:
 - (A) NAME: INFECTIO DIAGNOSTIC (I.D.I.) INC.
 - (B) STREET: 2050, BOULEVARD RENE LEVESQUE OUEST, 4E ETAGE
 - (C) CITY: STE-FOY
 - (D) STATE: QUEBEC
 - (E) COUNTRY: CANADA
 - (F) POSTAL CODE (ZIP): G1V 2K8
 - (G) TELEPHONE: (418) 681-4343
 - (H) TELEFAX: (418) 681-5254
 - (A) NAME: BERGERON, MICHEL G.
 - (B) STREET: 2069 RUE BRULARD
 - (C) CITY: SILLERY
 - (D) STATE: QUEBEC
 - (E) COUNTRY: CANADA
 - (F) POSTAL CODE (ZIP): G1T 1G2
 - (A) NAME: PICARD, FRANCOIS J.
 - (B) STREET: 1245, RUE DE LA SAPINIERE
 - (C) CITY: CAP-ROUGE
 - (D) STATE: QUEBEC
 - (E) COUNTRY: CANADA
 - (F) POSTAL CODE (ZIP): G1Y 1A1
 - (A) NAME: OUELLETTE, MARC
 - (B) STREET: 1035 DE PLOERMEL
 - (C) CITY: SILLERY
 - (D) STATE: QUEBEC
 - (E) COUNTRY: CANADA
 - (F) POSTAL CODE (ZIP): G1S 3S1
 - (A) NAME: ROY, PAUL H.
 - (B) STREET: 28, RUE CHARLES GARNIER
 - (C) CITY: LORETTEVILLE
 - (D) STATE: QUEBEC
 - (E) COUNTRY: CANADA
 - (F) POSTAL CODE (ZIP): G2A 3S1
- (ii) TITLE OF INVENTION: SPECIES-SPECIFIC, GENIUS-SPECIFIC AND UNIVERSAL DNA PROBES AND AMPLIFICATION PRIMERS TO RAPIDLY DETECT AND IDENTIFY COMMON BACTERIAL AND FUNGAL PATHOGENS AND ASSOCIATED ANTIBIOTIC RESISTANCE GENES ...
- (iii) NUMBER OF SEQUENCES: 174
- (iv) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)
- (vi) PRIOR APPLICATION DATA:

- 72 -

		(A) APPLICATION NUMBER: US 08/743,637 (B) FILING DATE: 04-NOV-1996	
(2)	INFO	RMATION FOR SEQ ID NO: 1:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Enterococcus faecium	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 1:	
TGCI	TTAG	CA ACAGCCTATC AG	22
(2)	INFO	RMATION FOR SEQ ID NO: 2:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
		ORIGINAL SOURCE: (A) ORGANISM: Enterococcus faecium	
11.	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 2:	
TAAA	CTTC	TT CCGGCACTTC G	21
(2)	INFO	RMATION FOR SEQ ID NO: 3:	
٠.	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Listeria monocytogenes	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 3:	
TGCG	GCTA	TA AATGAAGAGG C	21
(2)	TNFO	RMATION FOR SEO ID NO: 4:	

	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Listeria monocytogenes	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 4:	
ATCC	GATG	AT GCTATGGCTT T	21
(2)	INFO	RMATION FOR SEQ ID NO: 5:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Neisseria meningitidis	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 5:	
CCAG	CGGT	AT TGTTTGGTGG T	21
(2)	INFO	RMATION FOR SEQ ID NO: 6:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Neisseria meningitidis	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 6:	
CAGO	GCGC	CT TTAATAATTT C	21
(2)	INFO	RMATION FOR SEQ ID NO: 7:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	

	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Staphylococcus saprophyticus	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 7:	
AGAT	rcgaa'	IT CCACATGAAG GTTATTATGA	30
(2)	INFO	RMATION FOR SEQ ID NO: 8:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Staphylococcus saprophyticus	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 8:	
TCGC	CTTCT	CC CTCAACAATC AAACTATCCT	30
(2)	INFO	RMATION FOR SEQ ID NO: 9:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Streptococcus agalactiae	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 9:	
TTTC	CACCAC	GC TGTATTAGAA GTA	23
(2)	INFO	RMATION FOR SEQ ID NO: 10:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Streptococcus agalactiae	

- 75 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:	
GTTCCCTGAA CATTATCTTT GAT	23
(2) INFORMATION FOR SEQ ID NO: 11:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Candida albicans</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:	
CAAGAAGGTT GGTTACAACC CAAAGA	26
(2) INFORMATION FOR SEQ ID NO: 12:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(vi) ORIGINAL SOURCE: (A) ORGANISM: Candida albicans	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:	
AGGTCTTACC AGTAACTTTA CCGGAT	26
(2) INFORMATION FOR SEQ ID NO: 13:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:	
TACTGACAAA CCATTCATGA TG	22
(2) INFORMATION FOR SEQ ID NO: 14:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs	

- 76 -

	(B) TYPE: nucleic acid (C) STRANDEDNESS: single	
	(D) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:	
AACT	TTCGTCA CCAACGCGAA C	21
(2)	INFORMATION FOR SEQ ID NO: 15:	
	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:	
CTG	GCGCGGT ATGGTCGGTT	20
(2)	INFORMATION FOR SEQ ID NO: 16:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:	
GCCG	GACGTTG GAAGTGGTAA AG	22
(2)	INFORMATION FOR SEQ ID NO: 17:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:	
CCGI	TGTTGAA CGTGGTCAAA TCAAA	25
(2)	INFORMATION FOR SEQ ID NO: 18:	
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs	

- 77 -

(B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:	
TRTGTGGTGT RATWGWRCCA GGAGC	25
(2) INFORMATION FOR SEQ ID NO: 19:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:	
ACAACGTGGW CAAGTWTTAG CWGCT	25
(2) INFORMATION FOR SEQ ID NO: 20:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:	
ACCATTTCWG TACCTTCTGG TAAGT	25
(2) INFORMATION FOR SEQ ID NO: 21:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
<pre>(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:12 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:	
GAAATTGCAG GNAAATTGAT TGA	23

- 78 -

(2) INFORMATION FOR SEQ ID NO: 22: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:12 (D) OTHER INFORMATION:/note= "n = inosine" (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22: TTACGCATGG CNTGACTCAT CAT 23 (2) INFORMATION FOR SEQ ID NO: 23: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 3 (D) OTHER INFORMATION:/note= "n = inosine" (ix) FEATURE: (A) NAME/KEY: misc feature (B) LOCATION:6 (D) OTHER INFORMATION:/note= "n = inosine" (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 9 (D) OTHER INFORMATION:/note= "n = inosine" (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:12 (D) OTHER INFORMATION: /note= "n = inosine" (ix) FEATURE:

SUBSTITUTE SHEET (RULE 26)

(D) OTHER INFORMATION:/note= "n = inosine"

(A) NAME/KEY: misc feature

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

(B) LOCATION:15

- 79 **-**

ACNI	KKNACI	NG GNGTNGARAT GTT	23
(2)	INFO	RMATION FOR SEQ ID NO: 24:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:6 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:9 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:12 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	, ,	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:18 (D) OTHER INFORMATION:/note= "n = inosine" SEQUENCE DESCRIPTION: SEQ ID NO: 24:</pre>	
ΔVR'		NC CNGGCATNAC CAT	23
		RMATION FOR SEQ ID NO: 25:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 10 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 25:	
TCG	CTTCT	CC	10
(2)	INFO	RMATION FOR SEQ ID NO: 26:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 600 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double	

(D)	TOPOLOGY:	linear
-----	-----------	--------

- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Enterococcus faecium
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

TTCTTAGAGA CATTGAATAT GCCTTATGTC GGCGCAGGCG TATTGACCAG TGCATGTGCC 60 ATGGATAAAA TCATGACCAA GTATATTTTA CAAGCTGCTG GTGTGCCGCA AGTTCCTTAT 120 GTACCAGTAC TTAAGAATCA ATGGAAAGAA AATCCTAAAA AAGTATTTGA TCAATGTGAA 180 GGTTCTTTGC TTTATCCGAT GTTTGTCAAA CCTGCGAATA TGGGTTCTAG TGTCGGCATT 240 ACAAAGGCAG AAAACCGAGA AGAGCTGCAA AATGCTTTAG CAACAGCCTA TCAGTATGAT 300 TCTCGAGCAA TCGTTGAACA AGGAATTGAA GCGCGCGAAA TCGAAGTTGC TGTATTAGGA 360 AATGAAGATG TTCGGACGAC TTTGCCTGGC GAAGTCGTAA AAGACGTAGC ATTCTATGAT 420 TATGAAGCCA AATATATCAA TAATAAAATC GAAATGCAGA TTCCAGCCGA AGTGCCGGAA 480 GAAGTTTATC AAAAAGCGCA AGAGTACGCG AAGTTAGCTT ACACGATGTT AGGTGGAAGC 540 GGATTGAGCC GGTGCGATTT CTTTTTGACA AATAAAAATG AATTATTCCT GAATGAATTA 600

- (2) INFORMATION FOR SEQ ID NO: 27:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1920 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Listeria monocytogenes
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

GTGGGATTAA ACAGATTTAT GCGTGCGATG ATGGTGGTTT TCATTACTGC CAATTGCATT 60

ACGATTAACC CCGACATAAT ATTTGCAGCG ACAGATAGCG AAGATTCTAG TCTAAACACA 120

GATGAATGGG AAGAAGAAA AACAGAAGAG CAACCAAGCG AGGTAAATAC GGGACCAAGA 180

TACGAAACTG CACGTGAAGT AAGTTCACGT GATATTAAAG AACTAGAAAA ATCGAATAAA 240

GTGAGAAATA CGAACAAAGC AGACCTAATA GCAATGTTGA AAGAAAAAGC AGAAAAAGGT 300

CCAAATATCA ATAATAACAA CAGTGAACAA ACTGAGAATG CGGCTATAAA TGAAGAGGCT 360

TCAGGAGCCG	ACCGACCAGC	TATACAAGTG	GAGCGTCGTC	ATCCAGGATT	GCCATCGGAT	420
AGCGCAGCGG	AAATTAAAAA	AAGAAGGAAA	GCCATAGCAT	CATCGGATAG	TGAGCTTGAA	480
AGCCTTACTT	ATCCGGATAA	ACCAACAAAA	GTAAATAAGA	AAAAAGTGGC	GAAAGAGTCA	540
GTTGCGGATG	CTTCTGAAAG	TGACTTAGAT	TCTAGCATGC	AGTCAGCAGA	TGAGTCTTCA	600
CCACAACCTT	TAAAAGCAAA	CCAACAACCA	TTTTTCCCTA	AAGTATTTAA	AAAAATAAAA	660
GATGCGGGGA	AATGGGTACG	TGATAAAATC	GACGAAAATC	CTGAAGTAAA	GAAAGCGATT	720
GTTGATAAAA	GTGCAGGGTT	AATTGACCAA	TTATTAACCA	AAAAGAAAAG	TGAAGAGGTA	780
AATGCTTCGG	ACTTCCCGCC	ACCACCTACG	GATGAAGAGT	TAAGACTTGC	TTTGCCAGAG	840
ACACCAATGC	TTCTTGGTTT	TAATGCTCCT	GCTACATCAG	AACCGAGCTC	ATTCGAATTT	900
CCACCACCAC	CTACGGATGA	AGAGTTAAGA	CTTGCTTTGC	CAGAGACGCC	AATGCTTCTT	960
GGTTTTAATG	CTCCTGCTAC	ATCGGAACCG	AGCTCGTTCG	AATTTCCACC	GCCTCCAACA	1020
GAAGATGAAC	TAGAAATCAT	CCGGGAAACA	GCATCCTCGC	TAGATTCTAG	TTTTACAAGA	1080
GGGGATTTAG	CTAGTTTGAG	AAATGCTATT	AATCGCCATA	GTCAAAATTT	CTCTGATTTC	1140
CCACCAATCC	CAACAGAAGA	AGAGTTGAAC	GGGAGAGGCG	GTAGACCAAC	ATCTGAAGAA	1200
TTTAGTTCGC	TGAATAGTGG	TGATTTTACA	GATGACGAAA	ACAGCGAGAC	AACAGAAGAA	1260
GAAATTGATC	GCCTAGCTGA	TTTAAGAGAT	AGAGGAACAG	GAAAACACTC	AAGAAATGCG	1320
GGTTTTTTAC	CATTAAATCC	GTTTGCTAGC	AGCCCGGTTC	CTTCGTTAAG	TCCAAAGGTA	1380
TCGAAAATAA	GCGACCGGGC	TCTGATAAGT	GACATAACTA	AAAAAACGCC	ATTTAAGAAT	1440
CCATCACAGC	CATTAAATGT	GTTTAATAAA	AAAACTACAA	CGAAAACAGT	GACTAAAAA	1500
CCAACCCCTG	TAAAGACCGC	ACCAAAGCTA	GCAGAACTTC	CTGCCACAAA	ACCACAAGAA	1560
ACCGTACTTA	GGGAAAATAA	AACACCCTTT	ATAGAAAAAC	AAGCAGAAAC	AAACAAGCAG	1620
TCAATTAATA	TGCCGAGCCT	ACCAGTAATC	CAAAAAGAAG	CTACAGAGAG	CGATAAAGAG	1680
GAAATGAAAC	CACAAACCGA	GGAAAAAATG	GTAGAGGAAA	GCGAATCAGC	TAATAACGCA	1740
AACGGAAAAA	ATCGTTCTGC	TGGCATTGAA	GAAGGAAAAC	TAATTGCTAA	AAGTGCAGAA	1800
GACGAAAAAG	CGAAGGAAGA	ACCAGGGAAC	CATACGACGT	TAATTCTTGC	AATGTTAGCT	1860
ATTGGCGTGT	TCTCTTTAGG	GGCGTTTATC	AAAATTATTC	AATTAAGAAA	AATTAATTAA	1920
(-)	. 					

(2) INFORMATION FOR SEQ ID NO: 28:

(A) LENGTH: 415 base pairs

⁽i) SEQUENCE CHARACTERISTICS:

(B)	TYPE: nucleic	acid
(C)	STRANDEDNESS:	double

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Neisseria meningitidis
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

TACCGGTACG CTAAATATTG GTGATGTATT GGATATTATG ATTTGGGAAG CGCCGCCAGC 60

GGTATTGTTT GGTGGGCC TTTCTTCGAT GGGCTCGGGT AGTGCGCAAC AAACCAAGTT 120

GCCGGAGCAA CTGGTGACGG CACGTGGTAC GGTTTCTGTG CCGTTTGTTG GCGATATTTC 180

GGTGGTCGGT AAAACGCCTG GTCAGGTTCA GGAAATTATT AAAGGCCGCC TGAAAAAAAT 240

GGCCAATCAG CCGCAAGTGA TGGTGCGCTT GGTGCAGAAT AATGCGGCAA ATGTATCGGT 300

GATTCGCGCA GGCAATAGTG TGCGTATGCC GTTGACGGCA GCCGGTGAGC GTGTGTTGGA 360

TGCGGTGGCT GCGGTAGGTG AAATGTGCA GATACGAATG TGCAG 415

- (2) INFORMATION FOR SEQ ID NO: 29:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 438 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Staphylococcus saprophyticus
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

TCGCTTCTCC	AGAAGAAATT	TTAGAAACAT	ATCTAGAAAA	TCCCAAATTA	GATAAACCGT	60
TTATATTATG	TGAATACGCA	CATGCAATGG	GAAATTCACC	AGGAGATCTT	AATGCATATC	120
AAACATTAAT	TGAAAAATAT	GATAGTTTTA	TTGGCGGTTT	TGTTTGGGAA	TGGTGTGATC	180
ATAGCATTCA	GGTTGGGATA	AAGGAAGGTA	AACCAATTTT	TAGATATGGT	GGAGATTTTG	240
GTGAGGCCTT	ACATGACGGT	AATTTTTGTG	TTGATGGTAT	TGTTTCGCCA	GATCGAATTC	300
CACATGAAGG	TTATTATGAG	TTTAAACATG	AACATAGACC	TTTGAGATTG	GTTAACGAAG	360
AGGATTATCG	GTTTACATTG	AAGAATCAAT	TTGATTTTAC	AAATGCGGAG	GATAGTTTGA	420
TTGTTGAGGG	AGAAGCGA					438

(2) INFORMATION	FOR	SEQ	ID	NO:	30:
----	---------------	-----	-----	----	-----	-----

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 768 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus agalactiae
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

ATGAACGTTA CACATATGAT GTATCTATCT GGAACTCTAG TGGCTGGTGC ATTGTTATTT 60 TCACCAGCTG TATTAGAAGT ACATGCTGAT CAAGTGACAA CTCCACAAGT GGTAAATCAT 120 GTAAATAGTA ATAATCAAGC CCAGCAAATG GCTCAAAAGC TTGATCAAGA TAGCATTCAG 180 TTGAGAAATA TCAAAGATAA TGTTCAGGGA ACAGATTATG AAAAACCGGT TAATGAGGCT 240 ATTACTAGCG TGGAAAAATT AAAGACTTCA TTGCGTGCCA ACCCTGAGAC AGTTTATGAT 300 TTGAATTCTA TTGGTAGTCG TGTAGAAGCC TTAACAGATG TGATTGAAGC AATCACTTTT 360 TCAACTCAAC ATTTAACAAA TAAGGTTAGT CAAGCAAATA TTGATATGGG ATTTGGGATA 420 ACTAAGCTAG TTATTCGCAT TTTAGATCCA TTTGCTTCAG TTGATTCAAT TAAAGCTCAA 480 GTTAACGATG TAAAGGCATT AGAACAAAAA GTTTTAACTT ATCCTGATTT AAAACCAACT 540 GATAGAGCTA CCATCTATAC AAAATCAAAA CTTGATAAGG AAATCTGGAA TACACGCTTT 600 ACTAGAGATA AAAAAGTACT TAACGTCAAA GAATTTAAAG TTTACAATAC TTTAAATAAA 660 GCAATCACAC ATGCTGTTGG AGTTCAGTTG AATCCAAATG TTACGGTACA ACAAGTTGAT 720 CAAGAGATTG TAACATTACA AGCAGCACTT CAAACAGCAT TAAAATAA 768

- (2) INFORMATION FOR SEQ ID NO: 31:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 421 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Neisseria meningitidis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

ATGAAAGTAG GTTTCGTCGG CTGGCGCGGT ATGGTCGGTT CGGTTTTGAT GCAGCGTATG	60
AAAGAAGAAA ACGACTTCGC CCACATTCCC GAAGCGTTTT TCTTTACCAC TTCCAACGTC	120
GGCGGCGCAC GCCCTGATTT CGGTCAGGCG GCTAAAACAT TATTGGACGC GAACAACGTT	180
GCCGAGCTGG CAAAAATGGA CATCATCGTT ACCTGCCAAG GCGGCGACTA CACCAAATCC	240
GTCTTCCAAG CCCTGCGCGA CAGCGGCTGG AACGGCTACT GGATTGACGC GGCATCCTCG	300
CTGCGTATGA AAGACGACGC GATTATCGTC CTCGACCCCG TCAACCGCAA CGTCATCGAC	360
AACGGCCTCA AAAACGGCGT GAAAAACTAC ATCGGCGGCA ACTGTACCGT TTCCCTGATG	420
С	421
(2) INFORMATION FOR SEQ ID NO: 32:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 213 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Streptococcus gordonii</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:	
TTCATAGACG CTGAGCACGC TTTGGATCCA TCTTACGCGG CTGCTCTAGG TGTAAATATT	60
GATGAGCTGT TGCTATCTCA ACCAGATTCT GGTGAGCAAG GTTTAGAAAT TGCAGGAAAA	120
TTGATTGACT CTGGGGCAGT TGATTTAGTT GTCATCGACT CTGTTGCAGC TCTTGTACCA	180
CGTGCGGAAA TCGATGGAGA TATCGGTGAT AGC	213
(2) INFORMATION FOR SEQ ID NO: 33:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 692 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Streptococcus mutans</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:	

GGGCCGGAAT CTTCTGGTAA GACAACTGTC GCTCTTCATG CTGCTGCTCA GGCGCAAAAA 60

GATGGCGGTA	TTGCCGCTTT	CATTGATGCA	GAACATGCCC	TTGATCCAGC	CTATGCTGCT	120
GCTCTTGGCG	TTAATATTGA	TGAGCTTTTG	CTTTCACAAC	CAGATTCAGG	AGAACAGGGT	180
CTTGAAATTG	CAGGGAAATT	GATTGATTCT	GGCGCTGTTG	ATTTAGTTGT	TGTTGACTCA	240
GTGGCAGCTT	TAGTACCACG	TGCGGAGATT	GACGGAGATA	TTGGTAATAG	TCATGTTGGC	300
TTACAAGCAC	GCATGATGAG	TCAAGCGATG	CGTAAATTAT	CAGCTTCAAT	CAATAAAACA	360
AAAACCATTG	CTATTTTAT	TAATCAATTG	CGGGAAAAAG	TTGGTATTAT	GTTTGGTAAT	420
CCAGAAACAA	CCCTGGCGG	GCGTGCCTTG	AAGTTTTATT	CTTCTGTGCG	TCTTGATGTC	480
CGCGGCAATA	CTCAAATTAA	AGGAACCGGG	GAACAAAAG	ACAGCAATAT	TGGTAAAGAG	540
ACCAAAATTA	AAGTTGTTAA	AAATAAAGTT	GCTCCACCAT	TTAAGGAAGC	TTTTGTAGAA	600
ATTATATATG	GTGAAGGCAT	TTCTCGTACA	GGTGAATTAG	TTAAGATTGC	CAGTGATTTG	660
GGAATTATCC	AAAAAGCTGG	AGCTTGGTAC	TC			692

- (2) INFORMATION FOR SEQ ID NO: 34:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1204 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus pneumoniae
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

ATGGCGAAAA	AACCAAAAA	ATTAGAAGAA	ATTTCAAAAA	AATTTGGGGC	AGAACGTGAA	60
AAGGCCTTGA	ATGACGCTCT	TAAATTGATT	GAGAAAGACT	TTGGTAAAGG	ATCAATCATG	120
CGTTTGGGTG	AACGTGCGGA	GCAAAAGGTG	CAAGTGATGA	GCTCAGGTTC	TTTAGCTCTT	180
GACATTGCCC	TTGGCTCAGG	TGGTTATCCT	AAGGGACGTA	TCATCGAAAT	CTATGGCCCA	240
GAGTCATCTG	GTAAGACAAC	GGTTGCCCTT	CATGCAGTTG	CACAAGCGCA	AAAAGAAGGT	300
GGGATTGCTG	CCTTTATCGA	TGCGGAACAT	GCCCTTGATC	CAGCTTATGC	TGCGGCCCTT	360
GGTGTCAATA	TTGACGAATT	GCTCTTGTCT	CAACCAGACT	CAGGAGAGCA	AGGTCTTGAG	420
ATTGCGGGAA	AATTGATTGA	CTCAGGTGCA	GTTGATCTTG	TCGTAGTCGA	CTCAGTTGCT	480
GCCCTTGTTC	CTCGTGCGGA	AATTGATGGA	GATATCGGAG	ATAGCCATGT	TGGTTTGCAG	540
GCTCGTATGA	TGAGCCAGGC	CATGCGTAAA	CTTGGCGCCT	CTATCAATAA	AACCAAAACA	600

ATTGCCATTT	TTATCAACCA	ATTGCGTGAA	AAAGTTGGAG	TGATGTTTGG	AAATCCAGAA	660
ACAACACCGG	GCGGACGTGC	TTTGAAATTC	TATGCTTCAG	TCCGCTTGGA	TGTTCGTGGT	720
AATACACAAA	TTAAGGGAAC	TGGTGATCAA	AAAGAAACCA	ATGTCGGTAA	AGAAACTAAG	780
ATTAAGGTTG	AATAAAAAT	GGTAGCTCCA	CCGTTTAAGG	AAGCCGTAGT	TGAAATTATG	840
TACGGAGAAG	GAATTTCTAA	GACTGGTGAG	CTTTTGAAGA	TTGCAAGCGA	TTTGGATATT	900
ATCAAAAAAG	CAGGGGCTTG	GTATTCTTAC	AAAGATGAAA	AAATTGGGCA	AGGTTCTGAG	960
AATGCTAAGA	AATACTTGGC	AGAGCACCCA	GAAATCTTTG	ATGAAATTGA	TAAGCAAGTC	1020
CGTTCTAAAT	TTGGCTTGAT	TGATGGAGAA	GAAGTTTCAG	AACAAGATAC	TGAAAACAAA	1080
AAAGATGAGC	CAAAGAAAGA	AGAAGCAGTG	AATGAAGAAG	TTCCGCTTGA	CTTAGGCGAT	1140
GAACTTGAAA	TCGAAATTGA	AGAATAAGCT	GTTAAAGCAG	TGGAGAAATC	CGCTACTTTT	1200
TCGA						1204

(2) INFORMATION FOR SEQ ID NO: 35:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 981 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus pyogenes
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

ATGCGTTCAG GAAGTCTAGC TCTTGATATT GCTTGGATAG CTGGTGGTTA TCCTAAAGGA 60 CGTATCATCG AAATCTATGG TCCAGAGTCT TCCGGTAAAA CGACTGTGGC TTTACATGCT 120 GTAGCACAAG CTCAAAAAGA AGGTGGAATC GCAGCCTTTA TCGATGCCGA GCATGCGCTT 180 GATCCAGCTT ATGCTGCTGC GCTTGGGGTT AATATTGATG AACTTCTCTT GTCTCAACCA 240 GATTCTGGAG AACAAGGACT TGAAATTGCA GGTAAATTGA TTGATTCTGG TGCGGTTGAC 300 CTGGTTGTTG TCGATTCAGT AGCAGCTTTA GTGCCACGTG CTGAAATTGA TGGTGATATT 360 GGCGATAGCC ATGTCGGATT GCAAGCACGT ATGATGAGTC AGGCCATGCG TAAATTATCA 420 GCTTCTATTA ATAAAACAAA AACTATCGCA ATCTTTATCA ACCAATTGCG TGAAAAAGTT 480 GGTGTGATGT TTGGAAATCC TGAAACAACA CCAGGTGGTC GAGCTTTGAA ATTCTATGCT 540 TCTGTTCGGC TGGATGTGCG TGGAAACAAC CAAATTAAAG GAACTGGTGA CCAAAAGATA 600

- 87 -

GCCAGCATTG GTAAGGAGAC CAAAATCAAG GTTGTTAAAA ACAAGGTCGC TCCGCCATTT	660
AAGGTAGCAG AAGTTGAAAT CATGTATGGG GAAGGTATTT CTCGTACAGG GGAGCTTGTG	720
AAAATTGCTT CTGATTTGGA CATTATCCAA AAAGCAGGTG CTTGGTTCTC TTATAATGGT	780
GAGAAGATTG GCCAAGGTTC TGAAAATGCT AAGCGTTATT TGGCCGATCA TCCACAATTG	840
TTTGATGAAA TCGACCGTAA AGTACGTGTT AAATTTGGTT TGCTTGAAGA AAGCGAAGAA	900
GAATCTGCTA TGGCAGTAGC ATCAGAAGAA ACCGATGATC TTGCTTTAGA TTTAGATAAT	960
GGTATTGAAA TTGAAGATTA A	981
(2) INFORMATION FOR SEQ ID NO: 36:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 312 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(vi) ORIGINAL SOURCE:(A) ORGANISM: Streptococcus salivarius	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:	
GCGTATGCAC GAGCTCTAGG TGTTAATATC GATGAGCTTC TTTTGTCGCA GCCTGATTCT	60
GGTGAGCAAG GTCTCGAAAT TGCAGGTAAG CTGATTGACT CTGGTGCAGT GGATTTAGTT	120
GTTGTTGACT CAGTTGCGGC CTTCGTACCA CGTGCAGAAA TTGATGGAGA TAGTGGTGAC	180
AGTCATGTAG GACTTCAAGC GCGTATGATG AGTCAAGCCA TGCGTAAACT TTCTGCATCT	240
ATTAATAAAA CAAAAACGAT TGCTATCTTT ATTAACCAGT TGCGTGAAAA AGTTGGTATC	300
ATGTTTGGTA AC	312
(2) INFORMATION FOR SEQ ID NO: 37:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:	
CTATGTGGCG CGGTATTATC	20

(2) INFORMATION FOR SEQ ID NO: 38:

WO 98/20157

(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:	
CGCAGTGTTA TCACTCATGG	20
(2) INFORMATION FOR SEQ ID NO: 39:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:	
CTGAATGAAG CCATACCAAA	20
(2) INFORMATION FOR SEQ ID NO: 40:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:	
ATCAGCAATA AACCAGCCAG	20
(2) INFORMATION FOR SEQ ID NO: 41:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:	
TTACCATGAG CGATAACAGC	20
(2) INFORMATION FOR SEQ ID NO: 42:	

- 89 -

(i) SEQUENCE CHARACTERISTICS:

(2) INFORMATION FOR SEQ ID NO: 46:

(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:	
CTCATTCAGT TCCGTTTCCC	20
(2) INFORMATION FOR SEQ ID NO: 43:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:	
CAGCTGCTGC AGTGGATGGT	20
(2) INFORMATION FOR SEQ ID NO: 44:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:	
CGCTCTGCTT TGTTATTCGG	20
(2) INFORMATION FOR SEQ ID NO: 45:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:	
TACGCCAACA TCGTGGAAAG	20

WO 98/20157

(i) SEQUENCE CHARACTERISTICS:

- 90 -

	(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:	
TTG	ATTTGG CTTCTTCGGT	20
(2)	INFORMATION FOR SEQ ID NO: 47:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:	
GGGZ	TACAGA AACGGGACAT	20
(2)	INFORMATION FOR SEQ ID NO: 48:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:	
TAAI	TCTTTT TCAGGCAGCG	20
(2)	INFORMATION FOR SEQ ID NO: 49:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:	
GAT	GTTTGA AGGGTTTATT ATAAG	25
(2)	INFORMATION FOR SEQ ID NO: 50:	

- - - - -

- 91 -

(A) LENGTH: 25 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:	
AATTTAGTGT GTTTAGAATG GTGAT	25
(2) INFORMATION FOR SEQ ID NO: 51:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:	
ACTTCAACAC CTGCTGCTTT C	21
(2) INFORMATION FOR SEQ ID NO: 52:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:	
TGACCACTTT TATCAGCAAC C	21
(2) INFORMATION FOR SEQ ID NO: 53:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:	
GGCAATAGTT GAAATGCTCG	20
(2) INFORMATION FOR SEQ ID NO: 54:	

- 92 **-**

 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:	
CAGCTGTTAC AACGGACTGG	20
(2) INFORMATION FOR SEQ ID NO: 55:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:	
TCTATGATCT CGCAGTCTCC	20
(2) INFORMATION FOR SEQ ID NO: 56:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:	
ATCGTCACCG TAATCTGCTT	20
(2) INFORMATION FOR SEQ ID NO: 57:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:	
CATTCTCGAT TGCTTTGCTA	20
(2) INFORMATION FOR SEQ ID NO: 58:	

	(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:	
CCGF	AAATGCT TCTCAAGATA	20
(2)	INFORMATION FOR SEQ ID NO: 59:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:	
CTGG	GATTATG GCTACGGAGT	20
(2)	INFORMATION FOR SEQ ID NO: 60:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:	
AGC	AGTGTGA TGGTATCCAG	20
(2)	INFORMATION FOR SEQ ID NO: 61:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:	
GACT	PCTTGAT GAAGTGCTGG	20
(2)	INFORMATION FOR SEQ ID NO: 62:	

(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:	
CTGGTCTATT CCTCGCACTC	20
(2) INFORMATION FOR SEQ ID NO: 63:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:	
TATGAGAAGG CAGGATTCGT	20
(2) INFORMATION FOR SEQ ID NO: 64:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:	
GCTTTCTCTC GAAGGCTTGT	20
(2) INFORMATION FOR SEQ ID NO: 65:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:	
GAGTTGCTGT TCAATGATCC	20
(2) INFORMATION FOR SEQ ID NO: 66:	

- 95 -

	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 66:	
GTGT	TTGA/	AC CATGTACACG	20
(2)	INFO	RMATION FOR SEQ ID NO: 67:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 67:	
TGTA	GAGG'	TC TAGCCCGTGT	20
(2)	INFO	RMATION FOR SEQ ID NO: 68:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 68:	
ACGG	GGAT	AA CGACTGTATG	20
(2)	INFO	RMATION FOR SEQ ID NO: 69:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 69:	
ATAA	AGAT	GA TAGGCCGGTG	20
(2)	INFO	RMATION FOR SEQ ID NO: 70:	

(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:	
TGCTGTCATA TTGTCTTGCC	20
(2) INFORMATION FOR SEQ ID NO: 71:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:	
ATTATCTTCG GCGGTTGCTC	20
(2) INFORMATION FOR SEQ ID NO: 72:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:	
GACTATCGGC TTCCCATTCC	20
(2) INFORMATION FOR SEQ ID NO: 73:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:	
CGATAGAAGC AGCAGGACAA	20
(2) INFORMATION FOR SEQ ID NO: 74:	

(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:	
CTGATGGATG CGGAAGATAC	20
(2) INFORMATION FOR SEQ ID NO: 75:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:	
GCCTTATGTA TGAACAAATG G	21
(2) INFORMATION FOR SEQ ID NO: 76:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 23 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:	
GTGACTTTWG TGATCCCTTT TGA	23
(2) INFORMATION FOR SEQ ID NO: 77:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:	
TCCAATCATT GCACAAAATC	20
(2) INFORMATION FOR SEQ ID NO: 78:	

(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:	
AATTCCCTCT ATTTGGTGGT	20
(2) INFORMATION FOR SEQ ID NO: 79:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:	
TCCCAAGCCA GTAAAGCTAA	20
(2) INFORMATION FOR SEQ ID NO: 80:	
(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:	
TGGTTTTCA ACTTCTTCCA	20
(2) INFORMATION FOR SEQ ID NO: 81:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:	
TCATAGAATG GATGGCTCAA	20
(2) INFORMATION FOR SEQ ID NO: 82:	

 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:	
AGCTACTATT GCACCATCCC	20
(2) INFORMATION FOR SEQ ID NO: 83:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:	
CAATAAGGGC ATACCAAAAA TC	22
(2) INFORMATION FOR SEQ ID NO: 84:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:	
CCTTAACATT TGTGGCATTA TC	22
(2) INFORMATION FOR SEQ ID NO: 85:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:	
TTGGGAAGAT GAAGTTTTTA GA	22

(2) INFORMATION FOR SEQ ID NO: 86:

WO 98/20157 PCT/CA97/00829⁻

- 100 -

(A) LENGTH: 22 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:	
CCTTTACTCC AATAATTTGG CT	22
(2) INFORMATION FOR SEQ ID NO: 87:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:	
TTTCATCTAT TCAGGATGGG	20
(2) INFORMATION FOR SEQ ID NO: 88:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:	
GGAGCAACAT TCTTTGTGAC	20
(2) INFORMATION FOR SEQ ID NO: 89:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:	
TGTGCCTGAA GAAGGTATTG	20
(2) INFORMATION FOR SEQ ID NO: 90:	

	(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:	
CGTG	TTACTT CACCACCACT	20
(2)	INFORMATION FOR SEQ ID NO: 91:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:	
TATC	TTATCG TTGAGAAGGG ATT	23
(2)	INFORMATION FOR SEQ ID NO: 92:	
	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 22 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:	
CTAC	ACTTGG CTTAGGATGA AA	22
(2)	INFORMATION FOR SEQ ID NO: 93:	
	 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:	
CTAT	CTGATT GTTGAAGAAG GATT	24
(2)	INFORMATION FOR SEQ ID NO: 94:	

- 102 -

(A) LENGTH: 24 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:	
GTTTACTCTT GGTTTAGGAT GAAA	24
(2) INFORMATION FOR SEQ ID NO: 95:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:	
CTTGTTGATC ACGATAATTT CC	22
(2) INFORMATION FOR SEQ ID NO: 96:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:	
ATCTTTTAGC AAACCCGTAT TC	22
(2) INFORMATION FOR SEQ ID NO: 97:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:	
AACAGGTGAA TTATTAGCAC TTGTAAG	27
(2) INFORMATION FOR SEQ ID NO: 98:	

	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 98:	
ATTO	GCTGT	TA ATATTTTTG AGTTGAA	27
(2)	INFO	RMATION FOR SEQ ID NO: 99:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 19 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 99:	
GTG	ATCGA	AA TCCAGATCC	19
(2)	INFO	RMATION FOR SEQ ID NO: 100:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 19 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 100:	
ATC	CTCGG	IT TTCTGGAAG	19
(2)	INFO	RMATION FOR SEQ ID NO: 101:	
		SEQUENCE CHARACTERISTICS: (A) LENGTH: 19 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 101:	
CTG	STCAT	AC ATGTGATGG	19
(2)	INFO	RMATION FOR SEQ ID NO: 102:	

 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 19 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:	
GATGTTACCC GAGAGCTTG	19
(2) INFORMATION FOR SEQ ID NO: 103:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:	
TTAAGCGTGC ATAATAAGCC	20
(2) INFORMATION FOR SEQ ID NO: 104:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:	
TTGCGATTAC TTCGCCAACT	20
(2) INFORMATION FOR SEQ ID NO: 105:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:	
TTTACTAAGC TTGCCCCTTC	20
(2) INFORMATION FOR SEQ ID NO: 106:	

- 105 -

	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 106:	
AAAA	AGGCA	GC AATTATGAGC	20
(2)	INFO	RMATION FOR SEQ ID NO: 107:	
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(ii)	MOLECULE TYPE: DNA (genomic)	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:9 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:12 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:15 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	(ix)	<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:18 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
		<pre>FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION:21 (D) OTHER INFORMATION:/note= "n = inosine"</pre>	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 107:	
AAYA	ATGAT:	NA CNGGNGCNGC NCARATGGA	29
(2)	INFO	RMATION FOR SEQ ID NO: 108:	
	(i)	SEQUENCE CHARACTERISTICS:	

(A) LENGTH: 23 base pairs(B) TYPE: nucleic acid

- 106 -

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:6
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:9
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:12
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

CCNACNGTNC KNCCRCCYTC RCG

23

- (2) INFORMATION FOR SEQ ID NO: 109:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION:6
 - (D) OTHER INFORMATION:/note= "n = inosine"
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:12
 - (D) OTHER INFORMATION:/note= "n = inosine"
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:15
 - (D) OTHER INFORMATION:/note= "n = inosine"
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature

- 107 -

- (B) LOCATION:18
- (D) OTHER INFORMATION:/note= "n = inosine"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

CARYTNATHG TNGCNGTNAA YAARATGGA

29

- (2) INFORMATION FOR SEQ ID NO: 110:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 831 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

ATGAAAAACA	CAATACATAT	CAACTTCGCT	ATTTTTTAA	TAATTGCAAA	TATTATCTAC	60
AGCAGCGCCA	GTGCATCAAC	AGATATCTCT	ACTGTTGCAT	CTCCATTATT	TGAAGGAACT	120
GAAGGTTGTT	TTTTACTTTA	CGATGCATCC	ACAAACGCTG	AAATTGCTCA	ATTCAATAAA	180
GCAAAGTGTG	CAACGCAAAT	GGCACCAGAT	TCAACTTTCA	AGATCGCATT	ATCACTTATG	240
GCATTTGATG	CGGAAATAAT	AGATCAGAAA	ACCATATTCA	AATGGGATAA	AACCCCCAAA	300
GGAATGGAGA	TCTGGAACAG	CAATCATACA	CCAAAGACGT	GGATGCAATT	TTCTGTTGTT	360
TGGGTTTCGC	AAGAAATAAC	CCAAAAAATT	AGATTAAATA	AAATCAAGAA	TTATCTCAAA	420
GATTTTGATT	ATGGAAATCA	AGACTTCTCT	GGAGATAAAG	AAAGAAACAA	CGGATTAACA	480
GAAGCATGGC	TCGAAAGTAG	CTTAAAAATT	TCACCAGAAG	AACAAATTCA	ATTCCTGCGT	540
AAAATTATTA	ATCACAATCT	CCCAGTTAAA	AACTCAGCCA	TAGAAAACAC	CATAGAGAAC	600
ATGTATCTAC	AAGATCTGGA	TAATAGTACA	AAACTGTATG	GGAAAACTGG	TGCAGGATTC	660
ACAGCAAATA	GAACCTTACA	AAACGGATGG	TTTGAAGGGT	TTATTATAAG	CAAATCAGGA	720
CATAAATATG	TTTTTGTGTC	CGCACTTACA	GGAAACTTGG	GGTCGAATTT	AACATCAAGC	780
ATAAAAGCCA	AGAAAAATGC	GATCACCATT	CTAAACACAC	TAAATTTATA	A	831

- (2) INFORMATION FOR SEQ ID NO: 111:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 846 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

(xi) S	SEOUENCE	DESCRIPTION:	SEO	ID	NO:	111:
--------	----------	--------------	-----	----	-----	------

TTGAAAAAGT	TAATATTTT	AATTGTAATT	GCTTTAGTTT	TAAGTGCATG	TAATTCAAAC	60
AGTTCACATG	CCAAAGAGTT	AAATGATTTA	GAAAAAAAT	ATAATGCTCA	TATTGGTGTT	120
TATGCTTTAG	ATACTAAAAG	TGGTAAGGAA	GTAAAATTTA	ATTCAGATAA	GAGATTTGCC	180
TATGCTTCAA	CTTCAAAAGC	GATAAATAGT	GCTATTTTGT	TAGAACAAGT	ACCTTATAAT	240
AAGTTAAATA	AAAAAGTACA	TATTAACAAA	GATGATATAG	TTGCTTATTC	TCCTATTTTA	300
GAAAAATATG	TAGGAAAAGA	TATCACTTTA	AAAGCACTTA	TTGAGGCTTC	AATGACATAT	360
AGTGATAATA	CAGCAAACAA	TAAAATTATA	AAAGAAATCG	GTGGAATCAA	AAAAGTTAAA	420
CAACGTCTAA	AAGAACTAGG	AGATAAAGTA	ACAAATCCAG	TTAGATATGA	GATAGAATTA	480
AATTACTATT	CACCAAAGAG	CAAAAAAGAT	ACTTCAACAC	CTGCTGCTTT	CGGTAAGACT	540
TTAAATAAAC	TTATCGCAAA	TGGAAAATTA	AGCAAAGAAA	ACAAAAAATT	CTTACTTGAT	600
TTAATGTTAA	ATAATAAAAG	CGGAGATACT	TTAATTAAAG	ACGGTGTTCC	AAAAGACTAT	660
AAGGTTGCTG	ATAAAAGTGG	TCAAGCAATA	ACATATGCTT	CTAGAAATGA	TGTTGCTTTT	720
GTTTATCCTA	AGGGCCAATC	TGAACCTATT	GTTTTAGTCA	TTTTTACGAA	TAAAGACAAT	780
AAAAGTGATA	AGCCAAATGA	TAAGTTGATA	AGTGAAACCG	CCAAGAGTGT	AATGAAGGAA	840
TTTTAA						846

(2) INFORMATION FOR SEQ ID NO: 112:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 555 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

ATGTCCGCGA GCACCCCCC CATAACTCTT CGCCTCATGA CCGAGCGCGA CCTGCCGATG 60

CTCCATGACT GGCTCAACCG GCCGCACATC GTTGAGTGGT GGGGTGGCGA CGAAGAGCGA 120

CCGACTCTTG ATGAAGTGCT GGAACACTAC CTGCCCAGAG CGATGGCGGA AGAGTCCGTA 180

ACACCGTACA TCGCAATGCT GGGCGAGGAA CCGATCGGCT ATGCTCAGTC GTACGTCGCG 240

CTCGGAAGCG GTGATGGCTG GTGGGAAGAT GAAACTGATC CAGGAGTGCG AGGAATAGAC 300

CAGTCTCTGG CTGACCCGAC ACAGTTGAAC AAAGGCCTAG GAACAAGGCT TGTCCGCGCT 360

	-	N 9	
_		117	_

CTCGTTGAAC	TACTGTTCTC	GGACCCCACC	GTGACGAAGA	TTCAGACCGA	CCCGACTCCG	420
AACAACCATC	GAGCCATACG	CTGCTATGAG	AAGGCAGGAT	TCGTGCGGGA	GAAGATCATC	480
ACCACGCCTG	ACGGGCCGGC	GGTTTACATG	GTTCAAACAC	GACAAGCCTT	CGAGAGAAAG	540
CGCGGTGTTG	CCTAA					555

- (2) INFORMATION FOR SEQ ID NO: 113:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 732 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

ATGAACCAGA AAAACCCTAA AGACACGCAA AATTTTATTA CTTCTAAAAA GCATGTAAAA 60 GAAATATTGA ATCACAGAA TATCAGTAAA CAAGACAACG TAATAGAAAT CGGATCAGGA 120 AAAGGACATT TTACCAAAGA GCTAGTCAAA ATGAGTCGAT CAGTTACTGC TATAGAAATT 180 GATGGAGGCT TATGTCAAGT GACTAAAGAA GCGGTAAACC CCTCTGAGAA TATAAAAGTG 240 ATTCAAACGG ATATTCTAAA ATTTTCCTTC CCAAAACATA TAAACTATAA GATATATGGT 300 AATATTCCTT ATAACATCAG TACGGATATT GTCAAAAGAA TTACCTTTGA AAGTCAGGCT 360 AAATATAGCT ATCTTATCGT TGAGAAGGGA TTTGCGAAAA GATTGCAAAA TCTGCAACGA 420 GCTTTGGGTT TACTATTAAT GGTGGAGATG GATATAAAAA TGCTCAAAAA AGTACCACCA 480 CTATATTTC ATCCTAAGCC AAGTGTAGAC TCTGTATTGA TTGTTCTTGA ACGACATCAA 540 CCATTGATTT CAAAGAAGGA CTACAAAAAG TATCGATCTT TTGTTTATAA GTGGGTAAAC 600 CGTGAATATC GTGTTCTTTT CACTAAAAAC CAATTCCGAC AGGCTTTGAA GCATGCAAAT 660 GTCACTAATA TTAATAAACT ATCGAAGGAA CAATTTCTTT CTATTTTCAA TAGTTACAAA 720 TTGTTTCACT AA 732

- (2) INFORMATION FOR SEQ ID NO: 114:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 738 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

- 110 -

(xi)	SEQUENCE	DESCRIPTION:	SEQ	ID	NO:	114:
------	----------	--------------	-----	----	-----	------

ATGAACAAAA	ATATAAAATA	TTCTCAAAAC	TTTTTAACGA	GTGAAAAAGT	ACTCAACCAA	60
ATAATAAAAC	AATTGAATTT	AAAAGAAACC	GATACCGTTT	ACGAAATTGG	AACAGGTAAA	120
GGGCATTTAA	CGACGAAACT	GGCTAAAATA	AGTAAACAGG	TAACGTCTAT	TGAATTAGAC	180
AGTCATCTAT	TCAACTTATC	GTCAGAAAAA	TTAAAATCGA	ATACTCGTGT	CACTTTAATT	240
CACCAAGATA	TTCTACAGTT	TCAATTCCCT	AACAAACAGA	GGTATAAAAT	TGTTGGGAAT	300
ATTCCTTACC	ATTTAAGCAC	ACAAATTATT	AAAAAGTGG	TTTTTGAAAG	CCATGCGTCT	360
GACATCTATC	TGATTGTTGA	AGAAGGATTC	TACAAGCGTA	CCTTGGATAT	TCACCGAACA	420
CTAGGGTTGC	TCTTGCACAC	TCAAGTCTCG	ATTCAGCAAT	TGCTTAAGCT	GCCAGCGGAA	480
TGCTTTCATC	CTAAACCAAG	AGTAAACAGT	GTCTTAATAA	AACTTACCCG	CCATACCACA	540
GATGTTCCAG	ATAAATATTG	GAAGCTATAT	ACGTACTTTG	TTTCAAAATG	GGTCAATCGA	600
GAATATCGTC	AACTGTTTAC	TAAAAATCAG	TTTCATCAAG	CAATGAAACA	CGCCAAAGTA	660
AACAATTTAA	GTACCGTTAC	TTATGAGCAA	GTATTGTCTA	TTTTTAATAG	TTATCTATTA	720
TTTAACGGGA	GGAAATAA					738

(2) INFORMATION FOR SEQ ID NO: 115:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 735 base pairs
- (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

ATGAACGAGA	AAATATAAA	ACACAGTCAA	AACTTTATTA	CTTCAAAACA	TAATATAGAT	60
AAAATAATGA	CAAATATAAG	ATTAAATGAA	CATGATAATA	TCTTTGAAAT	CGGCTCAGGA	120
AAAGGGCATT	TTACCCTTGA	ATTAGTACAG	AGGTGTAATT	TCGTAACTGC	CATTGAAATA	180
GACCATAAAT	TATGCAAAAC	TACAGAAAAT	AAACTTGTTG	ATCACGATAA	TTTCCAAGTT	240
TTAAACAAGG	ATATATTGCA	GTTTAAATTT	CCTAAAAACC	AATCCTATAA	AATATTTGGT	300
AATATACCTT	ATAACATAAG	TACGGATATA	ATACGCAAAA	TTGTTTTTGA	TAGTATAGCT	360
GATGAGATTT	ATTTAATCGT	GGAATACGGG	TTTGCTAAAA	GATTATTAAA	TACAAAACGC	420
TCATTGGCAT	TATTTTTAAT	GGCAGAAGTT	GATATTTCTA	TATTAAGTAT	GGTTCCAAGA	480

- 111 -

GAATATTTTC	ATCCTAAACC	TAGAGTGAAT	AGCTCACTTA	TCAGATTAAA	TAGAAAAAA	540
TCAAGAATAT	CACACAAAGA	TAAACAGAAG	TATAATTATT	TCGTTATGAA	ATGGGTTAAC	600
AAAGAATACA	AGAAAATATT	TACAAAAAAT	CAATTTAACA	ATTCCTTAAA	ACATGCAGGA	660
ATTGACGATT	TAAACAATAT	TAGCTTTGAA	CAATTCTTAT	CTCTTTTCAA	TAGCTATAAA	720
TTATTTAATA	AGTAA					735

- (2) INFORMATION FOR SEQ ID NO: 116:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1029 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

ATGAATAAAA	TAAAAGTCGC	AATTATCTTC	GGCGGTTGCT	CGGAGGAACA	TGATGTGTCG	60
GTAAAATCCG	CAATAGAAAT	TGCTGCGAAC	ATTAATACTG	AAAAATTCGA	TCCGCACTAC	120
ATCGGAATTA	CAAAAAACGG	CGTATGGAAG	CTATGCAAGA	AGCCATGTAC	GGAATGGGAA	180
GCCGATAGTC	TCCCCGCCAT	ATTCTCCCCG	GATAGGAAAA	CGCATGGTCT	GCTTGTCATG	240
AAAGAAAGAG	AATACGAAAC	TCGGCGTATT	GACGTGGCTT	TCCCGGTTTT	GCATGGCAAA	300
TGCGGGGAGG	ATGGTGCGAT	ACAGGGTCTG	TTTGAATTGT	CTGGTATCCC	CTATGTAGGC	360
TGCGATATTC	AAAGCTCCGC	AGCTTGCATG	GACAAATCAC	TGGCCTACAT	TCTTACAAAA	420
AATGCGGGCA	TCGCCGTCCC	CGAATTTCAA	ATGATTGAAA	AAGGTGACAA	ACCGGAGGCG	480
AGGACGCTTA	CCTACCCTGT	CTTTGTGAAG	CCGGCACGGT	CAGGTTCGTC	CTTTGGCGTA	540
ACCAAAGTAA	ACAGTACGGA	AGAACTAAAC	GCTGCGATAG	AAGCAGCAGG	ACAATATGAT	600
GGAAAAATCT	TAATTGAGCA	AGCGATTTCG	GGCTGTGAGG	TCGGCTGCGC	GGTCATGGGA	660
AACGAGGATG	ATTTGATTGT	CGGCGAAGTG	GATCAAATCC	GGTTGAGCCA	CGGTATCTTC	720
CGCATCCATC	AGGAAAACGA	GCCGGAAAAA	GGCTCAGAGA	ATGCGATGAT	TATCGTTCCA	780
GCAGACATTC	CGGTCGAGGA	ACGAAATCGG	GTGCAAGAAA	CGGCAAAGAA	AGTATATCGG	840
GTGCTTGGAT	GCAGAGGGCT	TGCTCGTGTT	GATCTTTTT	TGCAGGAGGA	TGGCGGCATC	900
GTTCTAAACG	AGGTCAATAC	CCTGCCCGGT	TTTACATCGT	ACAGCCGCTA	TCCACGCATG	960
GCGGCTGCCG	CAGGAATCAC	GCTTCCCGCA	CTAATTGACA	GCCTGATTAC	ATTGGCGATA	1020

- 112 -

GAGAGGTGA 1029

- (2) INFORMATION FOR SEQ ID NO: 117:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1031 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

ATGAAAAAA	TTGCCGTTTT	ATTTGGAGGG	AATTCTCCAG	AATACTCAGT	GTCACTAACC	60
TCAGCAGCAA	GTGTGATCCA	AGCTATTGAC	CCGCTGAAAT	ATGAAGTAAT	GACCATTGGC	120
ATCGCACCAA	CAATGGATTG	GTATTGGTAT	CAAGGAAACC	TCGCGAATGT	TCGCAATGAT	180
ACTTGGCTAG	AAGATCACAA	AAACTGTCAC	CAGCTGACTT	TTTCTAGCCA	AGGATTTATA	240
TTAGGAGAAA	AACGAATCGT	CCCTGATGTC	CTCTTTCCAG	TCTTGCATGG	GAAGTATGGC	300
GAGGATGGCT	GTATCCAAGG	ACTGCTTGAA	CTAATGAACC	TGCCTTATGT	TGGTTGCCAT	360
GTCGCTGCCT	CCGCATTATG	TATGAACAAA	TGGCTCTTGC	ATCAACTTGC	TGATACCATG	420
GGAATCGCTA	GTGCTCCCAC	TTTGCTTTTA	TCCCGCTATG	AAAACGATCC	TGCCACAATC	480
GATCGTTTTA	TTCAAGACCA	TGGATTCCCG	ATCTTTATCA	AGCCGAATGA	AGCCGGTTCT	540
TCAAAAGGGA	TCACAAAAGT	AACTGACAAA	ACAGCGCTCC	AATCTGCATT	AACGACTGCT	600
TTTGCTTACG	GTTCTACTGT	GTTGATCCAA	AAGGCGATAG	CGGGTATTGA	AATTGGCTGC	660
GGCATCTTAG	GAAATGAGCA	ATTGACGATT	GGTGCTTGTG	ATGCGATTTC	TCTTGTCGAC	720
GGTTTTTTTG	ATTTTGAAGA	GAAATACCAA	TTAATCAGCG	CCACGATCAC	TGTCCCAGCA	780
CCATTGCCTC	TCGCGCTTGA	ATCACAGATC	AAGGAGCAGG	CACAGCTGCT	TTATCGAAAC	840
TTGGGATTGA	CGGGTCTGGC	TCGAATCGAT	TTTTTCGTCA	CCAATCAAGG	AGCGATTTAT	900
TTAAACGAAA	TCAACACCAT	GCCGGGATTT	ACTGGGCACT	CCCGCTACCC	AGCTATGATG	960
GCGGAAGTCG	GGTTATCCTA	CGAAATATTA	GTAGAGCAAT	TGATTGCACT	GGCAGAGGAG	1020
GACAAACGAT	G					1031

- (2) INFORMATION FOR SEQ ID NO: 118:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 809 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double

- 113 -

PCT/CA97/00829 -

(D)	TOPOLOGY:	linear
-----	-----------	--------

- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Abiotrophia adiacens
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

TGGTGCTATC TTAGTAGTAT CTGCAGCTGA TGGTCCAATG CCTCAAACAC GTGAACACAT 60 CTTATTATCA CGTCAAGTAG GTGTTCCTTA CATCGTTGTA TTCTTAAACA AAGTTGACAT 120 GGTTGACGAT GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTATCAGA 180 ATACGATTC CCAGGCGATG ACACTCCAGT TGTTGCAGGT TCTGCTTTAC GCGCTTTAGA 240 AGGCGACGCT TCATACRAAG AAAAAATCTT AGAATTAATG GCTGCTGTTG ACGAATACAT 300 TCCAACTCCA GAACGYGACG TTGACAAACC ATTCATGATG CCAGTTGAAG ACGTGTTCTC 360 AATCACAGGT CGTGGTACTG TTGCTACAGG TCGTGTTGAA CGTGGACAAG TTCGTGTTGG 420 TGACGAAGTT GAAATCGTTG GTATTTCAGA AGAAACTTCA AAAACAACTG TAACTGGTGT 480 TGAAATGTTC CGTAAATTGT TAGACTACGC TGAAGCAGGG GATAACATTG GTACATTATT 540 ACGTGGTGTT ACACGTGACA ACATCGAACG TGGACAAGTT CTTGCTAAAC CAGGAACAAT 600 CACTCCACAT ACTAAATTCA AAGCTGAAGT TTACGTATTA ACTAAAGAAG AAGGTGGACG 660 TCATACTCCA TTCTTCTCTA ACTACCGTCC TCAATTCTAC TTCCGTACAA CAGACATCAC 720 TGGTGTTTGT GTGTTACCAG AAGGCGTTGA AATGGTAATG CCTGGTGATA ACGTAACTAT 780 GGAAGTTGAA TTAATTCACC CAGTAGCGA 809

- (2) INFORMATION FOR SEQ ID NO: 119:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Abiotrophia defectiva
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

CGGCGCGATC CTCGTTGTAT CTGCTGCTGA CGGCCCAATG CCACAAACTC GTGAACACAT 60
CCTCTTGTCT CGTCAAGTTG GTGTTCCTTA CATCGTAGTA TTCTTGAACA AAGTTGACAT 120

- 114 -

GGTTGACGAC	GAAGAATTGC	TCGAATTAGT	TGAAATGGAA	GTTCGTGACC	TCTTGTCTGA	180
ATACGACTTC	CCAGGCGACG	ACACTCCAGT	TATCGCTGGT	TCAGCTTTGA	AAGCTTTAGA	240
AGGCGACGCT	AACTACGAAG	CTAAAGTTTT	AGAATTGATG	GAACAAGTTG	ATGCTTACAT	300
TCCAGAACCA	GAACGTGACA	CTGACAAGCC	ATTCATGATG	CCAGTCGAAG	ACGTATTCTC	360
TATCACTGGT	CGTGGTACTG	TTGCAACTGG	TCGTGTTGAA	CGTGGTCAAG	TTCGCGTTGG	420
TGACGAAGTT	GAAATCGTTG	GTATCGAAGA	AGAAACTTCT	AAGACTACCG	TTACCGGTGT	480
TGAAATGTTC	CGTAAGTTAT	TGGATTACGC	TGAAGCTGGG	GACAACGTTG	GTACCTTGTT	540
ACGTGGTGTA	ACTCGTGACC	AAATCCAACG	TGGTCAAGTA	TTATCTAAAC	CAGGTTCAAT	600
CACTCCGYAC	ACTAAGTTCG	AAGCTGAAGT	GTACGTATTG	TCTAAAGAAG	AAGGTGGTCG	660
TCACACTCCA	TTCTTCTCTA	ACTACCGTCC	ACAATTCTAC	TTCCGTACAA	CTGACGTAAC	720
TGGTGTTGTT	ACTTTACCAG	AAGGTACTGA	AATGGTTATG	CCAGGCGACA	ACGTACAAAT	780
GGTTGTTGAA	TTGATCCACC	CAATCGCGAT	CGAAGAA			817

(2) INFORMATION FOR SEQ ID NO: 120:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 754 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Candida albicans
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

CTCTGTCAAA TGGGACAAAA ACAGATTTGA AGAAATCATC AAGGAAACCT CCAACTTCGT 60 CAAGAAGGTT GGTTACAACC CAAAGACTGT TCCATTCGTT CCAATCTCTG GTTGGAATGG 120 TGACAACWTG ATTGAASCAT CCACCAACTG TCCATGGTAC AAGGGTTGGG AAAAGGAAAC 180 CAAATCCGGT AAAGTTACTG GTAAGACCTT GTTAGAAGCT ATTGACGCTA TTGAACCACC 240 AACCAGACCA ACCGACAAAC CATTGAGATT GCCATTRCAA GATGTTTACA AGATCGGTGG 300 TATTGGTACT GTGCCAGTCG GTAGAGTTGA AACTGGTATC ATCAAAGCCG GTATGGTWGT 360 TACTTTCGCC CCAGCTGGTG TTACCACTGA AGTCAARTCC GTTGAAATGC ATCACGAACA 420 ATTGGCTGAA GGTGTTCCAG GTGACAATGT TRGTTTCAAC GTTAAGAACR TTTCCGTTAA 480 AGAAATTAGA AGAGGTAACG TTTGTGGTGA CTCCAAGAAC GATCCACCAA AGGGTTGTGA 540

- 115 -

CTCTTTCAAT	GCCCAAGTCA	TTGTTTTGAA	CCATCCAGGT	CAAATCTCTG	CTGGTTACTC	600
TCCAGTCTTG	GATTGTCACR	CTGCCCACAT	TGCTTGTAAA	TTCGACRCTT	TGGTTGAAAA	660
GATTGACAGA	AGAACTGGTA	AGRAATTGGA	AGAAAATCCA	AAATTCGTCA	AATCCGGTGA	720
TGCTGCTATC	GTCAAGATGG	TCCCAACCAA	ACCA			754

- (2) INFORMATION FOR SEO ID NO: 121:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 753 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Candida glabrata
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

TCTGTCAAGT GGGATGAATC CAGATTCGCT GAAATCGTTA AGGAAACCTC CAACTTCATC 60 AAGAAGGTCG GTTACAACCC AAAGACTGTT CCATTCGTCC CAATCTCTGG TTGGAACGGT 120 GACAACATGA TTGAAGCCAC CACCAACGCT TCCTGGTACA AGGGTTGGGA AAAGGAAACC 180 AAGGCTGGTG TCGTCAAGGG TAAGACCTTG TTGGAAGCCA TTGACGCTAT CGAACCACCA 240 ACCAGACCAA CTGACAAGCC ATTGAGATTG CCATTGCAAG ATGTCTACAA GATCGGTGGT 300 ATCGGTACGG TGCCAGTCGG TAGAGTCGAA ACCGGTGTCA TCAAGCCAGG TATGGTTGTT 360 ACCTTCGCCC CAGCTGGTGT TACCACTGAA GTCAAGTCCG TTGAAATGCA CCACGAACAA 420 TTGACTGAAG GTTTGCCAGG TGACAACGTT GGTTTCAACG TTAAGAACGT TTCCGTTAAG 480 GAAATCAGAA GAGGTAATGT CTGTGGTGAC TCCAAGAACG ACCCACCAAA GGCTGCTGCT 540 TCTTTCAACG CTACCGTCAT TGTCTTGAAC CACCCAGGTC AAATCTCTGC TGGTTACTCT 600 CCAGTTTTGG ACTGTCACAC CGCCCACATT GCTTGTAAGT TCGAAGAATT GTTGGAAAAG 660 AACGACAGAA GATCCGGTAA GAAGTTGGAA GACTCTCCAA AGTTCTTGAA GTCCGGTGAC 720 GCTGCTTTGG TTAAGTTCGT TCCATCCAAG CCA 753

- (2) INFORMATION FOR SEQ ID NO: 122:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 752 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- 116 -

- 4		MOLECULE	FF7 2 25 25	T->-T-	/ \
	ייי) M()) H:('111 H:	J. A D B: •	DINA	- aenomici

- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Candida krusei
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

CCGTTAAGTG	GGATGAAAAC	AGATTTGAAG	AAATTGTCAA	GGAAACCCAA	AACTTCATCA	60
AGAAGGTTGG	TTACAACCCA	AAGACTGTTC	CATTCGTTCC	AATCTCTGGT	TGGAATGGTG	120
ACAACATGAT	TGAAGCATCC	ACCAACTGTC	CATGGTACAA	GGGTTGGACT	AAGGAAACCA	180
AGGCAGGTGT	TGTTAAGGGT	AAGACCTTAT	TAGAAGCAAT	CGATGCTATT	GAACCACCTG	240
TCAGACCAAC	CGAAAAGCCA	TTAAGATTAC	CATTACAAGA	TGTTTACAAG	ATTGGTGGTA	300
TTGGTACTGT	GCCAGTCGGT	AGAGTCGAAA	CCGGTGTCAT	TAAGCCAGGT	ATGGTTGTCA	360
CTTTTGCTCC	AGCAGGTGTC	ACCACCGAAG	TCAAATCCGT	TGAAATGCAC	CATGAACAAT	420
TAGAACAAGG	TGTTCCAGGT	GATAACGTTG	GTTTCAACGT	TAAGAACGTY	TCTGTCAAGG	480
ATATCAAGAG	AGGTAACGTT	TGTGGTGACT	CCAAGAACGA	CCCACCAATG	GGTGCAGCTT	540
CTTTCAATGC	TCAAGTCATT	GTCTTGAACC	ACCCTGGTCA	AATTTCCGCT	GGTTACTCTC	600
CAGTCTTGGA	TTGTCACACT	GCCCACATTG	CATGTAAGTT	CGACGAATTA	ATCGAAAAGA	660
TTGACAGAAG	AACTGGTAAG	TCTGTTGAAG	ACCATCCAAA	GTCYGTCAAG	TCTGGTGATG	720
CAGCTATCGT	CAAGATGGTC	CCAACCAAGC	CA			752

(2) INFORMATION FOR SEQ ID NO: 123:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 754 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Candida parapsilosis
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

CTCAGTCAAA TGGGACAAGA RCAGATACGA AGAAATTGTC AAGGAAACTT CCAACTTCGT 60

CAAGAAGGTT GGTTACAACC CTAAAGCTGT CCCATTCGTC CCAATCTCTG GTTGGAACGG 120

TGACAATATG ATTGAACCAT CAACCAACTG TCCATGGTAC AAGGGTTGGG AAAAGGAAAC 180

TAAAGCTGGT AAGGTTACCG GTAAGACCTT GTTGGAAGCT ATCGATGCTA TCGARCCACC 240

- **117** -

AACCAGACCA	ACTGACAAGC	CATTGAGATT	GCCATTGCAA	GATGTCTACA	AGATTGGTGG	300
TATTGGAACT	GTGCCAGTTG	GTAGAGTTGA	AACCGGTATC	ATCAAGGCTG	GTATGGTTGT	360
TACTTTTGCC	CCAGCTGGTG	TTACCACTGA	AGTCAAGTCC	GTTGAAATGC	ACCACGAACA	420
ATTGACTGAA	GGTGTCCCAG	GTGACAATGT	TGGTTTCAAC	GTCAAGAACG	TTTCAGTTAA	480
GGAAATCAGA	AGAGGTAACG	TYTGTGGTGA	CTCCAAGAAC	GATCCACCAA	AGGGATGTGA	540
YTCCTTCAAT	GCTCAAGTTA	TTGTCTTGAA	CCACCCAGGT	CAAATCTCTG	CTGGTTACTC	600
ACCAGTCTTG	GATTGTCACA	CTGCCCACAT	TGCTTGTAAA	TTCGACACTT	TGATTGAAAA	660
GATTGACAGA	AGAACCGGTA	AGAAATTGGA	AGWTGAACCA	AAATTCATCA	AGTCCGGTGA	720
TGCTGCYATC	GTCAAGATGG	TCCCAACCAA	GCCA			754

- (2) INFORMATION FOR SEQ ID NO: 124:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 753 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Candida tropicalis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

TCTGTTAAAT	GGGACAARAA	CAGATTTGAA	GAAATTATCA	AGGAAACYTC	TAACTTCGTC	60
AAGAAGGTTG	GTTACAACCC	TAAGGCTGTT	CCATTCGTTC	CAATCTCWGG	TTGGAATGGT	120
GACAACATGA	TTGAAGCTTC	TACCAACTGT	CCATGGTACA	AGGGTTGGGA	AAAAGAAACC	180
AAGGCTGGTA	AGGTTACCGG	TAAGACTTTG	TTGGAAGCCA	TTGATGCTAT	TGAACCACCT	240
TCAAGACCAA	CTGACAAGCC	ATTGAGATTG	CCATTGCAAG	ATGTTTACAA	GATTGGTGGT	300
ATTGGTACTG	TGCCAGTCGG	TAGAGTTGAA	ACTGGTGTCA	TCAAAGCCGG	TATGGTTGTT	360
ACTTTYGCCC	CAGCTGGTGT	TACCACTGAA	GTCAAATCCG	TYGAAATGCA	CCACGAACAA	420
TTGGCTGAAG	GTGTCCCAGG	TGACAATGTT	GGTTTCAACG	TTAAGAACGT	TTCTGTTAAA	480
GAAATTAGAA	GAGGTAACGT	TTGTGGTGAC	TCCAAGAACG	ATCCACCAAA	GGGTTGTGAC	540
TCTTTCAACG	CTCAAGTTAT	TGTCTTGAAC	CACCCAGGTC	AAATYTCTGC	TGGTTACTCT	600
CCAGTCTTGG	ATTGTCACAC	TGCTCATATT	GCTTGTAAAT	TCGACACCTT	GGTTGAAAAG	660
ATTGACAGAA	GAACTGGTAA	GAAATTGGAA	GAAAATCCAA	AATTCGTCAA	ATCCGGTGAT	720

- 118 -

GCTGCTATTG TCAAGATGGT TCCAACCAAA CCA

753

- (2) INFORMATION FOR SEQ ID NO: 125:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 814 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Corynebacterium accolens
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

CGGCGCTATC	CTGGTTGTTG	CTGCAACCGA	TGGCCCGATG	CCGCAGACCC	GCGAGCACGT	60
TCTGCTTGCT	CGCCAGGTTG	GCGTTCCTTA	CATCCTCGTT	GCACTGAACA	AGTGCGACAT	120
GGTTGATGAT	GAGGAAATCA	TCGAGCTCGT	GGAGATGGAG	ATCTCCGAGC	TGCTCGCAGA	180
GCAGGACTAC	GATGAGGAAG	CTCCTATCGT	TCACATCTCC	GCTCTGAAGG	CACTCGAGGG	240
TGACGAGAAG	TGGGTACAGT	CCATCGTTGA	CCTGATGGAT	GCCTGCGACA	ACTCCATCCC	300
TGATCCGGAG	CGCGCTACCG	ATCAGCCGTT	CTTGATGCCT	ATCGAGGACA	TCTTCACCAT	360
TACCGGCCGC	GGTACCGTTG	TTACCGGCCG	TGTTGAGCGT	GGTCGTCTGA	ACGTCAACGA	420
GGACGTTGAG	ATCATCGGTA	TCCAGGAGAA	GTCCCAGAAC	ACCACCGTTA	CCGGTATCGA	480
GATGTTCCGC	AAGATGATGG	ACTACACCGA	GGCTGGCGAC	AACTGTGGTC	TGCTTCTGCG	540
TGGTACCAAG	CGTGAGGACG	TTGAGCGTGG	CCAGGTTGTT	ATCAAGCCGG	GCGCTTACAC	600
CCCTCACACC	AAGTTCGAGG	GTTCCGTCTA	CGTCCTGAAG	AAGGAAGAGG	GCGGCCGCCA	660
CACCCCGYTC	ATGAACAACT	ACCGTCCTCA	GTTCTACTTC	CGCACCACCG	ACGTTACCGG	720
TGTTGTGAAC	CTGCCTGAGG	GCACCGAGAT	GGTTATGCCT	GGCGACAACG	TTGAGATGTC	780
TGTTGAGCTC	ATCCAGCCTG	TTGCTATGGA	CGAG			814

- (2) INFORMATION FOR SEQ ID NO: 126:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 814 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:

- 119 -

(A) ORGANISM: Corynebacterium diphteriae

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

CGGCGCAATC	CTCGTTGTTG	CTGCCACCGA	CGGCCCAATG	CCTCAGACCC	GTGAGCACGT	60
TCTGCTCGCT	CGCCAGGTCG	GCGTTCCTTA	CATCCTCGTT	GCTCTGAACA	AGTGCGACAT	120
GGTTGATGAT	GAGGAAATCA	TCGAGCTCGT	CGAGATGGAG	ATCCRTGAGC	TGCTCGCTGA	180
GCAGGATTAC	GACGAAGAGG	CTCCAATCAT	CCACATCTCC	GCACTGAAGG	CTCTTGAGGG	240
CGACGAGAAG	TGGACCCAGT	CCATCATCGA	CCTCATGCAG	GCTTGCKATG	ATTCCATCCC	300
AGACCCAGAG	CGTGAGACCG	ACAAGCCATT	CCTCATGCCT	ATCGAGGACA	TCTTCACCAT	360
CACCGGCCGC	GGTACCGTTG	TTACCGGCCG	TGTTGAGCGT	GGCTCCCTGA	AGGTCAACGA	420
GGACGTCGAG	ATCATCGGTA	TCCGCGAGAA	KGCTACCACC	ACCACCGTTA	CCGGTATCGA	480
GATGTTCCGT	AAGCTTCTCG	ACTACACCGA	GGCTGGCGAC	AACTGTGGTC	TGCTTCTCCG	540
TGGCGTTAAG	CGCGAAGACG	TTGAGCGTGG	CCAGGTTGTT	GTTAAGCCAG	GCGCTTACAC	600
CCCTCACACC	GAGTTCGAGG	GCTCTGTCTA	CGTTCTGTCC	AAGGACGAGG	GTGGCCGCCA	660
CACCCCATTC	TTCGACAACT	ACCGCCCACA	GTTCTACTTC	CGCACCACCG	ACGTTACCGG	720
TGTTGTGAAG	CTTCCTGAGG	GCACCGAGAT	GGTCATGCCT	GGCGACAACG	TCGACATGTC	780
CGTCACCCTG	ATCCAGCCTG	TCGCTATGGA	TGAG			814

(2) INFORMATION FOR SEQ ID NO: 127:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 814 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Corynebacterium genitalium
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

CGGCGCCATC CTGGTTGTTG CTGCAACCGA TGGCCCGATG CCGCAGACCC GTGAGCACGT 60

TCTGCTGGCT CGCCAGGTTG GCGTTCCGTA CATCCTAGTT GCACTGAACA AGTGCGACAT 120

GGTTGATGAT GAGGAGCTGC TGGAGCTCGT CGAGATGGAG GTCCGCGAGC TGCTGGCTGA 180

GCAGGACTTC GACGAGGAAG CACCTGTTGT TCACATCTCC GCACTGAAGG CCCTGGAGGG 240

CGACGAGAAG TGGGCTAAGC AGATCCTGGA GCTCATGGAG GCTTGCGACA ACTCCATCCC 300

- 120 -

GGATCCGGAG	CGCGAGACCG	ACAAGCCGTT	CCTGATGCCG	GTTGRGGACA	TCTTCACCAT	360
TACCGGCCGC	GGTACCGTTG	TTACCGGCCG	TGTTGAGCGT	GGCGTCCTGA	ACCTGAACGA	420
CGAGGTCGAG	ATCCTGGGCA	TCCGCGAGAA	GTCCACCAAG	ACCACCGTTA	CCTCCATCGA	480
GATGTTCAAC	AAGCTGCTGG	ACACCGCAGA	GGCTGGCGAC	AACGCCGCAC	TGCTGCTGCG	540
TGGCCTGAAG	CGCGAAGATG	TTGAGCGTGG	TCAGATCGTT	GCTAAGCCGG	GCGAGTACAC	600
CCCGCACACC	GAGTTCGAGG	GCTCCGTCTA	CGTTCTGTCC	AAGGACGAGG	GTGGCCGCCA	660
CACCCCGTTC	TTCGACAACT	ACCGTCCGCA	GTTCTATTTC	CGCACCACCG	ACGTTACCGG	720
TGTTGTGAAG	CTGCCGGAGG	GCACCGAGAT	GGTTATGCCG	GGCGACAACG	TTGACATGTC	780
CGTCACCCTG	ATCCAGCCGG	TTGCTATGGA	CGAG			814

(2) INFORMATION FOR SEQ ID NO: 128:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 814 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Corynebacterium jeikeium
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

CGGCGCCATC	CTGGTTGTTG	CCGCAACCGA	TGGCCCGATG	CCGCAGACCC	GCGAGCACGT	60
TCTGCTGGCY	CGCCAGGTTG	GCGTTCCGTA	CATCCTGGTT	GCACTGAACA	AGTGTGACAT	120
GGTTGACGAT	GAGGAGCTGC	TGGAGCTCGT	CGAGATGGAG	GTCCGCGAGC	TGCTGGCTGA	180
GCAGGACTTC	GACGAGGAAG	CTCCGGTTGT	TCACATCTCC	GCACTGAAGG	CCCTGGAGGG	240
CGACGAGAAG	TGGGCTAACC	AGATTCTCGA	GCTGATGCAG	GCTTGCGACG	AGTCTATCCC	300
GGATCCGGAG	CGCGAGACCG	ACAAGCCGTT	CCTGATGCCG	GTTGWGGACA	TCTTCACCAT	360
TACCGGTCGC	GGTACCGTTG	TTACCGGCCG	TGTTGAGCGT	GGCATCCTGA	ACCTGAACGA	420
CGAGGTTGAG	ATCCTGGGTA	TCCGCGAGAA	GTCCCAGAAG	ACCACCGTTA	CCTCCATCGA	480
GATGTTCAAC	AAGCTGCTGG	ACACCGCAGA	GGCTGGCRAC	AACGCTGCAC	TGCTGCTGCG	540
TGGTCTGAAG	CGCGAGGACG	TTGAGCGTGG	CCAGATCATC	GCTAAGCCGG	GCGAGTACAC	600
CCCGCACACC	GAGTTCGAGG	GCTCCGTCTA	CGTTCTGTCC	AAGGACGAGG	GCGGCCGCCA	660
CACCCCGTTC	TTCGACAACT	ACCGTCCGCA	GTTCTACTTC	CGCACCACCG	ACGTTACCGG	720

WO 98/20157 PCT/CA97/00829

- 121 -

TGTTGTGAAG CTGCCTGAGG GCACCGAGAT GGTTATGCCG GGCGACAACG TYGACATGTC	780
CGTCACCCTG ATCCAGCCGG TTGCTATGGA CGAG	814
(2) INFORMATION FOR SEQ ID NO: 129:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 748 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
<pre>(vi) ORIGINAL SOURCE: (A) ORGANISM: Corynebacterium pseudodiphteriticum</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:	
CGGCGCTATC TTGGTTGTTG CAGCTACCGA CGGCCCAATG CCACAGACTC GCGAGCACGT	60
TCTGCTGGCT CGCCAGGTTG GCGTTCCTTA CATCCTGGTT GCACTAAACA AGTGCGACAT	120
GGTTGACGAC GAGGAAATCC TCGAGCTCGT CGAGATGGAG ATCCGCGAAT TGCTGGCTGA	180
CCAGGAATTC GACGAAGAAG CTCCAATCGT TCACATCTCC GCAGTCGGCG CCTTGGAAGG	240
CGAAGAGAGG TGGGTTAACG CCATCGTTGA ACTGATGGAT GCTTGTGACG AGTCGATCCC	300
TGATCCAGAC CGTGCTACCG ACAAGCCATT CCTGATGCCT ATCGAGGACA TCTTCACCAT	360
TACCGGTCGT GGCACCGTTG TTACGGGTCG TGTTGAGCGT GGTTCCCTGA AGGTCAACGA	420
AGAAGTCGAG ATCATCGGCA TCAAGGAAAA GTCCCAGAAG ACCACCATCA CCGGTATCGA	480
AATGTTCCGC AAGATGCTGG ACTACACCGA GGCCGGCGAC AACGCTGGTC TGCTGCTTCG	540
CGGTACCAAG CGTGAAGACG TTGAGCGTGG ACAGGTTATC GTTGCTCCAG GTGCTTACAG	600
CACCCACAG AAGTTCGAAG GTTCCGTCTA CGTTCTTTCC AAGGACGAGG GCGGCCGCCA	660
CACCCCGTTC TTCGACAACT ACCGTCCTCA GTTCTACTTC CGCACCACCG ACGTTACCGG	720
TGTTGTTACC CTGCCTGAGG GCACCGAG	748
(2) INFORMATION FOR SEQ ID NO: 130:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 813 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear 	

- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:

- 122 -

(A) ORGANISM: Corynebacterium striatum

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

GGCGCTATCT	TGGTTGTTGC	TGCAACCGAT	GGCCCGRTGC	CGCAGACCCG	CGAGCACGTT	60
CTTCTGGCTC	GCCAGGTTGG	CGTTCCTTAC	ATCCTCGTTG	CACTGAACAA	GTGCGACATG	120
GTTGACGACG	AGGAAATTAT	CGAGCTCGTC	GAGATGGAGA	TCCGCGAACT	GCTCGCAGAG	180
CAGGACTACG	ATGAGGAAGC	TCCGATCGTT	CACATCTCTG	CTCTGAAGGC	TCTTGAGGGC	240
GRCGAGAAGT	GGGTACAGGC	TATCGTTGAC	CTGATGCAGG	CTTGCGATGA	CTCCATCCCG	300
GATCCGGAGC	GCGAGCTGGA	CAAGCCGTTC	CTGATGCCAA	TCGAGGACAT	CTTCACCATC	360
ACCGGCCGCG	GTACCGTTGT	TACTGGCCGT	GTTGAGCGTG	GCTCCCTGAA	CGTCAACGAG	420
GACGTTGAGA	TCATCGGTAT	CCAGGACARG	TCCATCTCCA	CCACCGTTAC	CGGTATCGAG	480
ATGYTCCGCA	AGATGATGGA	CTACACCGAG	GCTGGCGACA	ACTGTGGTCT	GCTTCTGCGT	540
GGTACCAAGC	GTGAAGAGGT	TGAGCGCGGC	CAGGTTGTTA	TTAAGCCGGG	CGCTTACACC	600
CCTCACACCC	AGTTCGAGGG	TTCCGTCTAC	GTCCTGAAGA	AGGAAGAGGG	CGGCCGCCAC	660
ACCCCGTTCA	TGGACAACTA	CCGTCCGCAG	TTCTACTTCC	GCACCACCGA	CGTTACCGGC	720
GTCATCAAGC	TGCCTGAGGG	CACCGAGATG	GTTATGCCTG	GCGACAACGT	CGAGATGTCY	780
GTCGAGCTGA	TCCAGCCGGT	CGCTATGGAC	GAG			813

(2) INFORMATION FOR SEQ ID NO: 131:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Enterococcus avium
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

CGGAGCTATC	TTAGTAGTAT	CTGCTGCTGA	TGGCCCTATG	CCTCAAACTC	GTGAACACAT	60
CTTGTTATCT	CGTAACGTTG	GTGTTCCTTA	CATCGTTGTA	TTCTTAAACA	AAATGGATAT	120
GGTTGACGAT	GAAGAATTAC	TTGAATTAGT	TGAAATGGAA	GTTCGTGACT	TATTAACTGA	180
ATACGACTTC	CCAGGCGACG	ACACTCCAGT	TATCGCAGGT	TCAGCGTTGA	AAGCTTTAGA	240
AGGCGACGCT	TCATACGAAG	AAAAAATCTT	AGAATTAATG	GCTGCTGTTG	ACGAATATAT	300

the true

CCCAACACCA	GTTCGTGATA	CTGACAAACC	ATTCATGATG	CCAGTCGAAG	ACGTATTCTC	360
AATCACTGGT	CGTGGTACTG	TTGCAACTGG	TCGTGTTGAA	CGTGGACAAG	TTCGCGTTGG	420
TGACGAAGTT	GAAATCGTAG	GTATCGCTGA	CGAAACTGCT	AAAACAACTG	TTACAGGTGT	480
TGAAATGTTC	CGTAAATTGT	TAGACTACGC	TGAAGCAGGT	GACAACATCG	GTGCTTTGTT	540
ACGTGGTGTT	GCACGTGAAG	ATATCCAACG	TGGACAAGTA	TTGGCTAAAC	CAGCTTCAAT	600
CACTCCACAT	ACAAAATTCT	CTGCAGAAGT	TTATGTTCTA	ACTAAAGAAG	AAGGTGGACG	660
TCATACTCCA	TTCTTCACTA	ACTACCGTCC	TCAGTTCTAC	TTCCGTACAA	CTGACGTAAC	720
TGGTGTAGTT	GATCTACCAG	AAGGTACTGA	AATGGTWATG	CCTGGGGATA	ACGTAACTAT	780
GGAAGTTGAA	TTGATYCACC	CAATYGCGGT	AGAAGAC			817

- (2) INFORMATION FOR SEQ ID NO: 132:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Enterococcus faecalis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

CGGAGCTATC TTAGTAGTTT CTGCTGCTGA TGGTCCTATG CCTCAAACAC GTGAACATAT 60 CTTATTATCA CGTAACGTTG GTGTACCATA CATCGTTGTA TTCTTAAACA AAATGGATAT 120 GGTTGATGAC GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTATCAGA 180 ATACGATTTC CCAGGCGATG ATGTTCCAGT TATCGCAGGT TCTGCTTTGA AAGCTTTAGA 240 AGGCGACGAG TCTTATGAAG AAAAAATCTT AGAATTAATG GCTGCAGTTG ACGAATATAT 300 CCCAACTCCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTCGAAG ACGTATTCTC 360 AATCACTGGA CGTGGTACTG TTGCTACAGG ACGTGTTGAA CGTGGTGAAG TTCGCGTTGG 420 TGACGAAGTT GAAATCGTTG GTATTAAAGA CGAAACATCT AAAACAACYG TTACAGGTGT 480 TGAAATGTTC CGTAAATTAT TAGACTACGC TGAAGCAGGC GACAACMTCG GTGCTTTATT 540 ACGTGGTGTA GCACGTGAAG ATATCGAACG TGGACAAGTA TTAGCTAAAC CAGCTACAAT 600 CACTCCACAC ACAAAATTCA AAGCTGAAGT ATACGTATTA TCAAAAGAAG AAGGCGGACG 660 TCACACTCCA TTCTTCACTA ACTACCGTCC TCAATTCTAC TTCCGTACAA CAGACGTTAC 720 - 124 -

TGGTGTTGTA	GAATTGCCAG	AAGGTACTGA	AATGGTAATG	CCTGGTGATA	ACGTTGCTAT	780
GGACGTTGAA	TTAATTCACC	CAATCGCTAT	CGAAGAC			817

- (2) INFORMATION FOR SEQ ID NO: 133:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 774 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Enterococcus faecium
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

CGGAGCTATC TTGGTAGTTT CTGCTGCTGA CGGCCCAATG CCTCAAACTC GTGAACACAT 60 CCTATTGTCT CGTCAAGTTG GTGTTCCTTA CATCGTTGTA TTCTTGAACA AAGTAGACAT 120 GGTTGATGAC GAAGAATTAC TAGAATTAGT TGAAATGGAA GTTCGTGACC TATTAACAGA 180 ATACRAATTC CCTGGTGRCG ATGTTCCTGT AGTTGCTGGA TCAGCTTTGA AAGCTCTAGA 240 AGGCGACGCT TCATACGAAG AAAAAATTCT TGAATTAATG GCTGCAGTTG ACGAATACAT 300 CCCAACTCCA GAACGTGACA ACGACAAACC ATTCATGATG CCAGTTGAAG ACGTGTTCTC 360 AATTACTGGA CGTGGTACTG TTGCTACAGG TCGTGTTGAA CGTGGACAAG TTCGCGTTGG 420 TGACGAAGTT GAAGTTGTTG GTATTGCTGA AGAAACTTCA AAAACAACAG TTACTGGTGT 480 TGAAATGTTC CGTAAATTGT TAGACYACGC TGAAGCTGGA GACRACATTG GTGCTTTACT 540 ACGTGGTGTT GCACGTGAAG ACATCCAACG TGGACAAGTT TTAGCTAAAC CAGGTACAAT 600 CACACCTCRT ACAAAATTCT CTGCAGAAGT ATACGTGTTG ACAAAAGAAG AAGGTGGACG 660 TCATACTCCA TTCTTCACTA ACTACCGTCC ACAATTCTAC TTCCGTACAA CTGACGTAAC 720 AGGTGTTGTT GAATTACCAG AAGGAACTGA AATGGTCATG CCCGGTGACA ACGT 774

- (2) INFORMATION FOR SEQ ID NO: 134:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 809 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:

- 125 -

(A) ORGANISM: Enterococcus gallinarum

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134: CGGTGCGATC TTAGTAGTAT CTGCTGCTGA CGGTCCTATG CCTCAAACTC GTGAACACAT 60 CTTGTTATCA CGTAACGTTG GCGTACCATA CATCGTTGTT TTCTTGAACA AAATGGATAT 120 GGTTGAYGAC GAAGAATTGC TAGAATTAGT TGAAATGGAA GTTCGTGACC TATTGTCTGA 180 ATATGACTTC CCAGGCGACG ATGTTCCTGT AATCGCCGGT TCTGCTTTGA AAGCTCTTGA 240 AGGAGATCCT TCATACGAAG AAAAAATCAT GGAATTGATG GCTGCAGTTG ACGAATACGT 300 TCCAACTCCA GAACGTGATA CTGACAAACC ATTCATGATG CCAGTCGAAG ACGTATTCTC 360 AATCACTGGA CGTGGTACTG TTGCTACAGG CCGTGTTGAA CGTGGACAAG TTCGCGTTGG 420 TGATGAAGTA GAAATCGTTG GTATTGCTGA CGAAACTGCT AAAACAACTG TAACAGGTGT 480 TGAAATGTTC CGTAAATTGT TAGACTATGC TGAAGCAGGG GATAACATTG GTGCATTGCT 540 ACGTGGGGTT GCTCGTGAAG ACATCCAACG TGGACAAGTA TTGGCTAAAG CTGGTACAAT 600 CACACCTCAT ACAAAATTCA AAGCTGAAGT TTATGTTTTG ACAAAAGAAG AAGGTGGACG 660 TCACACTCCA TTCTTCACTA ACTACCGTCC TCAGTTCTAC TTCCGTACAA CTGACGTAAC 720 TGGTGTTGTT GAATTACCAG AAGGAACTGA AATGGTGATG CCTGGCGACA ACGTGACCAT 780

(2) INFORMATION FOR SEQ ID NO: 135:

CGACGTTGAA TTGATRCACC CAATCGCTC

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 823 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Gardnerella vaginalis
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

TGGCGCAATC CTCGTGGTTG CTGCTACCGA CGGTCCAATG GCTCAGACCC GTGAACACGT 60

CTTGCTTGCT AAGCAGGTCG GCGTTCCAAA AATTCTTGTT GCTTTGAACA AGTGCGATAT 120

GGTTGACGAC GAAGAGCTTA TCGATCTCGT TGAAGAAGAG GTCCGTGACC TCCTCGAAGA 180

AAACGGCTTC GATCGCGATT GCCCAGTCYT CCGTACTTCC GCTTACGGCG CTTTGCATGA 240

TGACGCTCCA GACCACGACA AGTGGGTAGA GACCGTCAAG GAACTCATGA AGGCTGTTGA 300

809

- 126 -

CGAGTACATC	CCAACCCCAA	CTCACGATCT	TGACAAGCCA	TTCTTGATGC	CAATCGAAGA	360
TGTGTTCACC	ATCTCCGGTC	GTGGTYCCGT	TGTCACCGGT	CGTGTTGAGC	GTGGTAAGCT	420
CCCAATCAAC	ACCCCAGTTG	AGATCGTTGG	TTTGCGCGAT	ACCCAGACCA	CCACCGTCAC	480
CTCTATCGAG	ACCTTCCACA	AGCAGATGGA	TGAGGCAGAG	GCTGGCGATA	ACACTGGTCT	540
TCTTCTCCGC	GGTATCAACC	GTACCGACGT	TGAGCGTGGT	CAGGTTGTGG	CTGCTCCAGG	600
TTCTGTGACT	CCACACACCA	AGTTCGAAGG	CGAAGTTTAC	GTCTTGACCA	AGGACGAAGG	660
TGGCCGTCAC	TCGCCATTCT	TCTCCAACTA	CCGTCCACAG	TTCTACTTCC	GTACCACCGA	720
TGTTACTGGC	GTTATCACCT	TGCCAGACGG	CATCGAAATG	GTTCAGCCAG	GCGATCACGC	780
AACCTTCACT	GTTGAGTTGA	TCCAGGCTAT	CGCAATGGAA	GAG		823

- (2) INFORMATION FOR SEQ ID NO: 136:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Listeria innocua
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

CGGAGCTATC	TTAGTAGTAT	CTGCTGCTGA	TGGCCCAATG	CCACAAACTC	GTGAACATAT	60
CTTACTTTCA	CGTCAAGTTG	GTGTTCCATA	CATCGTTGTA	TTCATGAACA	AATGTGACAT	120
GGTTGACGAT	GAAGAATTAC	TAGAATTAGT	TGAAATGGAA	ATTCGTGATC	TATTAACTGA	180
ATATGAATTC	CCTGGCGATG	ACATTCCTGT	AATCAAAGGT	TCAGCTCTTA	AAGCACTTCA	240
AGGTGAAGCT	GACTGGGAAG	CTAAAATTGA	CGAGTTAATG	GAAGCTGTAG	ATTCTTACAT	300
TCCAACTCCA	GAACGTGATA	CTGACAAACC	ATTCATGATG	CCAGTTGAGG	ATGTATTCTC	360
AATCACTGGT	CGTGGAACAG	TTGCAACTGG	ACGTGTTGAA	CGTGGACAAG	TTAAAGTTGG	420
TGACGAAGTA	GAAGTTATCG	GTATTGAAGA	AGAAAGCAAA	AAAGTAGTAG	TAACTGGAGT	480
AGAAATGTTC	CGTAAATTAC	TAGACTACGC	TGAAGCTGGC	GACAACATTG	GCGCACTTCT	540
ACGTGGTGTT	GCTCGTGAAG	ATATCCAACG	TGGTCAAGTA	TTAGCTAAAC	CAGGTTCGAT	600
TACTCCACAC	ACTAACTTCA	AAGCTGAAAC	TTATGTTTTA	ACTAAAGAAG	AAGGTGGACG	660
TCACACTCCA	TTCTTCAACA	ACTACCGCCC	ACAATTCTAT	TTCCGTACTA	CTGACGTAAC	720

- 127 -

TGGTATTGTT	ACACTTCCAG	AAGGTACTGA	AATGGTAATG	CCTGGTGATA	ACATTGAGCT	780
TGCAGTTGAA	CTAATTGCAC	CAATCGCTAT	CGAAGAC			817

- (2) INFORMATION FOR SEQ ID NO: 137:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 818 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Listeria ivanovii
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGTCCAATG CCACAAACTC GTGAACATAT 60 TCTTACTTTC ACGTCAAGTT GGTGTTCCAT ACATCGTTGT ATTCATGAAC AAATGTGACA 120 TGGTTGACGA TGAAGAATTA CTTGAATTAG TTGAAATGGA AATTCGTGAT CTATTAACTG 180 AATATGAATT CCCTGGCGAC GACATTCCTG TAATCAAAGG TTCAGCTCTT AAAGCACTTC 240 AAGGTGAAGC TGATTGGGAA GCTAAAATTG ACGAGTTAAT GGAAGCTGTA GATTCTTACA 300 TTCCAACTCC AGAACGTGAT ACTGACAAAC CATTCATGAT GCCAGTTGAG GATGTATTCT 360 CAATCACTGG TCGTGGAACA GTTGCAACTG GACGTGTTGA ACGTGGACAA GTTAAAGTTG 420 GTGACGAAGT AGAAGTTATC GGTATTGAAG AAGAAAGCAA AAAAGTAGTA GTAACTGGAG 480 TAGAAATGTT CCGTAAATTA CTAGACTACG CTGAAGCTGG CGACAACATT GGCGCACTTC 540 TACGTGGTGT TGCTCGTGAA GATATCCAAC GTGGTCAAGT ATTAGCTAAA CCAGGTTCGA 600 TTACTCCACA TACTAACTTC AAAGCTGAAA CTTATGTTTT AACTAAAGAA GAAGGTGGAC 660 GTCATACTCC ATTCTTCAAC AACTACCGCC CACAATTCTA TTTCCGTACT ACTGACGTAA 720 CTGGTATTGT TACACTTCCA GAAGGTACTG AAATGGTAAT GCCTGGTGAT AACATTGAGC 780 TTGCAGTTGA ACTAATTGCA CCAATCGCTA TCGAAGAC 818

- (2) INFORMATION FOR SEQ ID NO: 138:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

- 128 **-**

í	(351)	ORIGIN	JΔT.	SOTTRCE .
-	V 1 1	() (4 ((4 ((VAL.	OURCE:

(A) ORGANISM: Listeria monocytogenes

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

60	GTGAACATAT	CCACAAACTC	TGGCCCAATG	CTGCTGCTGA	TTAGTAGTAT	CGGAGCTATC
120	AATGTGACAT	TTCATGAACA	CATCGTTGTA	GTGTTCCATA	CGTCAAGTTG	CTTACTTTCA
180	TATTAACTGA	ATTCGTGATC	TGAAATGGAA	TAGAATTAGT	GAAGAATTAC	GGTTGACGAT
240	AAGCACTTCA	TCAGCTCTTA	AATCAAAGGT	ACATTCCTGT	CCTGGCGATG	ATATGAATTC
300	ATTCTTACAT	GAAGCTGTAG	CGAGTTAATG	CTAAAATTGA	GACTGGGAAG	aggtgaagct
360	ATGTATTCTC	CCAGTTGAGG	ATTCATGATG	CTGACAAACC	GAACGTGATA	TCCAACTCCW
420	TTAAAGTTGG	CGTGGACAAG	ACGTGTTGAA	TTGCAACTGG	CGTGGAACAG	AATCACTGGT
480	TAACTGGAGT	AAAGTAGTAG	AGAAAGCAAA	GTATCGAAGA	GAAGTTATCG	TGACGAAGTA
540	GCGCACTTCT	GACAACATTG	TGAAGCTGGC	TAGACTACGC	CGTAAATTAC	AGAAATGTTC
600	CAGGTTCGAT	TTAGCTAAAC	TGGTCAAGTA	ATATCCAACR	GCTCGTGAAG	ACGTGGTGTT
660	AAGGTGGACG	ACTAAAGAAG	TTATGTTTTA	AAGCTGAAAC	ACTAACTTCA	TACTCCACAC
720	CTGACGTAAC	TTCCGTACTA	ACAATTCTAT	ACTACCGCCC	TTCTTCAACA	TCACACTCCA
780	ACATTGAGCT	CCTGGTGATA	AATGGTAAYG	AAGGTACTGA	ACACTTCCAG	TGGTATTGTT
817			CGAAGAC	CAATCGCTAT	CTAATTGCAC	TGCAGTTGAA

(2) INFORMATION FOR SEQ ID NO: 139:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Listeria seeligeri
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACATAT 60

CTTACTTTCA CGTCAAGTTG GTGTTCCATA CATCGTTGTA TTCATGAACA AATGTGACAT 120

GGTTGACGAT GAAGAATTAC TTGAATTAGT TGAAATGGAA ATTCGTGATC TATTAACTGA 180

ATATGAATTC CCTGGTGATG ACATTCCTGT AATCAAAGGT TCAGCTCTTA AAGCACTTCA 240

- 129 -

AGGTGAAGCT	GACTGGGAAG	CTAAAATTGA	CGAGTTAATG	GAAGCTGTAG	ATTCTTACAT	300
TCCAACTCCA	GAACGTGATA	CTGACAAACC	ATTCATGATG	CCAGTTGAGG	ATGTATTCTC	360
AATCACTGGT	CGTGGAACTG	TTGCAACTGG	ACGTGTTGAA	CGTGGACAAG	TTAAAGTTGG	420
TGACGAAGTA	GAAGTTATCG	GTATTGAAGA	AGAAAGCAAA	AAAGTAATAG	TAACTGGAGT	480
AGAAATGTTC	CGTAAATTAC	TAGACTACGC	TGAAGCTGGC	GACAACATTG	GCGCACTTCT	540
ACGTGGTGTT	GCTCGTGAAG	ATATCCAACG	TGGTCAAGTA	TTAGCTAAAC	CAGGTTCGAT	600
TACTCCACAT	ACTAACTTCA	AAGCTGAAAC	TTATGTTTTA	ACTAAAGAAG	AAGGTGGACG	660
TCACACTCCA	TTCTTCAACA	ACTACCGCCC	ACAATTCTAT	TTCCGTACTA	CTGACGTAAC	720
TGGTATTGTT	ACACTTCCAG	AAGGTACTGA	AATGGTAATG	CCTGGTGATA	ACATTGAGCT	780
TGCAGTTGAA	CTAATTGCAC	CAATCGCTAT	CGAAGAC			817

(2) INFORMATION FOR SEQ ID NO: 140:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 814 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Staphylococcus aureus
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

CGGTGGTATC TTAGTAGTAT CTGCTGCTGA CGGTCCAATG CCACAAACTC GTGAACACAT 60 TCTTTTATCA CGTAACGTTG GTGTACCAGC ATTAGTAGTA TTCTTAAACA AAGTTGACAT 120 GGTTGACGAT GAAGAATTAT TAGAATTAGT AGAAATGGAA GTTCGTGACT TATTAAGCGA 180 ATATGACTTC CCAGGTGACG ATGTACCTGT AATCGCTGGT TCAGCATTAR AAGCTTTAGA 240 AGGCGATGCT CAATACGAAG AAAAAATCTT AGAATTARTG GAAGCTGTAG ATACTTACAT 300 TCCAACTCCA GAACGTGATT CTGACAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC 360 AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTTGAA CGTGGTCAAA TCAAAGTTGG 420 TGAAGAAGTT GAAATCATCG GTTTACATGA CACATCTAAA ACAACTGTTA CAGGTGTTGA 480 AATGTTCCGT AAATTATTAG ACTACGCTGA AGCTGGTGAC AACATTGGTG CATTATTACG 540 TGGTGTTGCT CGTGAAGACG TACAACGTGG TCAAGTATTA GCTGCTCCTG GTTCAATTAC 600 660 ACCACATACT GAATTCAAAG CAGAAGTATA CGTATTATCA AAAGACGAAG GTGGACGTCA

- 130 -

CACTCCATTC	TTCTCAAACT	ATCGTCCACA	ATTCTATTTC	CGTACTACTG	ACGTAACTGG	720
TGTTGTTCAC	TTACCAGAAG	GTACTGAAAT	GGTAATGCCT	GGTGATAACG	TTGAAATGAC	780
AGTAGAATTA	ATCGCTCCAA	TCGCGATTGA	AGAC			814

- (2) INFORMATION FOR SEQ ID NO: 141:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 814 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Staphylococcus epidermidis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

CGGCGGTATC	TTAGTTGTAT	CTGCTGCTGA	CGGTCCAATG	CCACAAACTC	GTGAACACAT	60
CTTATTATCA	CGTAACGTTG	GTGTACCAGC	ATTAGTTGTA	TTCTTAAACA	AAGTTGACAT	120
GGTAGACGAC	GAAGAATTAT	TAGAATTAGT	TGAAATGGAA	GTTCGTGACT	TATTAAGCGA	180
ATATGACTTC	CCAGGTGACG	ATGTACCTGT	AATCGCTGGT	TCTGCATTAA	AAGCATTAGA	240
AGGCGATGCT	GAATACGAAC	AAAAAATCTT	AGACTTAATG	CAAGCAGTTG	ATGATTACAT	300
TCCAACTCCA	GAACGTGATT	CTGACAAACC	ATTCATGATG	CCAGTTGAGG	ACGTATTCTC	360
AATCACTGGT	CGTGGTACTG	TTGCTACAGG	CCGTGTTGAA	CGTGGTCAAA	TCAAAGTWGG	420
TGAAGAAGTT	GAAATCATCG	GTATGCACGA	AACTTCTAAA	ACAACTGTTA	CTGGTGTAGA	480
AATGTTCCGT	AAATTATTAG	ACTACGCTGA	AGCTGGTGAC	AACATCGGTG	CTTTATTACG	540
TGGTGTTGCA	CGTGAAGACG	TACAACGTGG	TCAAGTATTA	GCTGCTCCTG	GTTCTATTAC	600
ACCACACACA	AAATTCAAAG	CTGAAGTATA	CGTATTATCT	AAAGATGAAG	GTGGACGTCA	660
CACTCCATTC	TTCACTAACT	ATCGCCCACA	ATTCTATTTC	CRTACTACTG	ACGTAACTGG	720
TGTTGTAAAC	TTACCAGAAG	GTACAGAAAT	GGTTATGCCT	GGCGACAACG	TTGAAATGAC	780
AGTTGAATTA	ATCGCTCCAA	TCGCTATCGA	AGAC			814

- (2) INFORMATION FOR SEQ ID NO: 142:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Staphylococcus saprophyticus
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

CGGAGCTATC TTAGTAGTAT CTGCTGCTGA TGGCCCAATG CCACAAACTC GTGAACACAT 60 TCTTTTATCA CGTRACGTTG GTGYTCCAGC ATTAGTTGTA TTCTTAAACA AAGTTGACAT 120 GGTTGACGAY GAAGAATTAT TAGAATTRGT AGAAATGGAA GTTCGTGRCT TATTAAGCGA 1.80 ATATGACTTC CCAGGTGACG ATGTACCTGT AATCTCTGGT TCTGCATTAA AAGCTTTAGA 240 AGGCGACGCT GACTATGAGC AAAAAATCTT AGACTTAATG CAAGCTGTTG ATGACTYCAT 300 TCCAACACCA GAACGTGATT CTGACAAACC ATTCATGATG CCAGTTGAGG ACGTATTCTC 360 AATCACTGGT CGTGGTACTG TTGCTACAGG CCGTGTTGAA CGTGGTCAAA TCAAAGTCGG 420 TGAAGAATC GARATCATCG GTATGCAAGA AGAATCAAGC AAAACAACTG TTACTGGTGT 480 AGAAATGTTC CGTAAATTAT TAGACTACGC TGAAGCTGGT GACAACATTG GTGCATTATT 540 ACGTGGTGTT TCACGTGATG ATGTACAACG TGGTCAAGTT TTAGCTGCTC CTGGTACTAT 600 CACACCACAT ACAAAATTCA AAGCGGATGT TTACGTTTTA TCTAAAGATG AAGGTGGTCG 660 TCATACGCCA TTCTTCACTA ACTACCGCCC ACAATTCTAT TTCCGTACTA CTGACGTAAC 720 TGGTGTTGTT AACTTACCAG AAGGTACTGA AATGGTTATG CCTGGCGATA ACGTTGAAAT 780 GGATGTTGAA TTAATTTCTC CAATCGCTAT TGAAGAC 817

- (2) INFORMATION FOR SEQ ID NO: 143:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Staphylococcus simulans
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

CGGCGGTATC TTAGTAGTAT CTGCTGCAGA TGGTCCAATG CCACAAACTC GTGAACACAT 60

CTTATTATCA CGTAACGTTG GTGTACCAGC TTTAGTTGTA TTCTTAAACA AAGCTGACAT 120

GGTTGACGAC GAAGAATTAT TAGAATTAGT TGAAATGGAA GTTCGTGACT TATTATCTGA 180

- 132 **-**

ATACGACTTC	CCTGGTGACG	ATGTACCAGT	TATCGTTGGT	TCTGCATTAA	AAGCTTTAGA	240
AGGCGACCCA	GAATACGAAC	AAAAAATCTT	AGACTTAATG	CAAGCTGTAG	ATGACTACAT	300
CCCAACTCCA	GAACGTGACT	CTGATAAACC	ATTCATGATG	CCAGTTGAGG	ACGTATTCTC	360
AATCACTGGT	CGTGGTACTG	TAGCAACAGG	CCGTGTTGAA	CGTGGTCAAA	TCAAAGTCGG	420
TGAAGAAGTT	GAAATCATCG	GTATCACTGA	AGAAAGCAAG	AAAACAACAG	TTACAGGTGT	480
AGAAATGTTC	CGTAAATTAT	TAGACTACGC	TGAAGCTGGT	GACAACATCG	GTGCTTTATT	540
ACGTGGTGTT	GCACGTGAAG	ACGTACAACG	TGGACAAGTA	TTAGCAGCTC	CTGGCTCTAT	600
TACTCCACAC	ACAAAATTCA	AAGCTGATGT	TTACGTTTTA	TCTAAAGAAG	AAGGTGGACG	660
TCATACTCCA	TTCTTCACTA	ACTACCGCCC	ACAATTCTAC	TTCCGTACTA	CTGACGTAAC	720
TGGCGTTGTT	CACTTACCAG	AAGGTACTGA	AATGGTTATG	CCTGGCGATA	ACGTAGAAAT	780
GACTGTTGAA	TTGATCGCTC	CAATCGCGAT	TGAAGAC			817

(2) INFORMATION FOR SEQ ID NO: 144:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus agalactiae
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

CGGAGCTATC CTTGTAGTTG CTTCAACTGA TGGACCAATG CCACAAACTC GTGAGCACAT 60 CCTTCTTTCA CGTCAAGTTG GTGTTAAACA CCTTATCGTA TTCATGAACA AAGTTGACCT 120 TGTTGATGAT GAAGAATTGC TTGAATTGGT TGAAATGGAA ATTCGTGACC TTCTTTCAGA 180 ATACGACTTC CCAGGTGATG ACCTTCCAGT TATCCAAGGT TCAGCTCTTA AAGCACTTGA 240 AGGCGACGAA AAATACGAAG ACATCATCAT GGAATTGATG AGCACTGTTG ATGAGTACAT 300 TCCAGAACCA GAACGTGATA CTGACAAACC TTTACTTCTT CCAGTTGAAG ATGTATTCTC 360 AATCACTGGA CGTGGTACAG TTGCTTCAGG ACGTATCGAC CGTGGTACTG TTCGTGTCAA 420 CGACGAAGTT GAAATCGTTG GTATTAAAGA AGATATCCAA AAAGCAGTTG TTACTGGTGT 480 TGAAATGTTC CGTAAACAAC TTGACGAAGG TCTTGCAGGG GACAACGTTG GTGTTCTTCT 540 TCGTGGTGTT CAACGTGATG AAATCGAACG TGGTCAAGTT CTTGCTAAAC CAGGTTCAAT 600

- 133 -

CAACCCACAC	ACTAAATTTA	AAGGTGAAGT	TTACATCCTT	TCTAAAGAAG	AAGGTGGACG	660
TCATACTCCA	TTCTTCAACA	ACTACCGTCC	ACAATTCTAC	TTCCGTACAA	CTGACGTAAC	720
AGGTTCAATC	GAACTTCCAG	CAGGAACAGA	AATGGTTATG	CCTGGTGATA	ACGTTACTAT	780
CGAAGTTGAA	TTGATTCACC	CAATCGCCGT	AGAACAA			817

- (2) INFORMATION FOR SEQ ID NO: 145:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus pneumoniae
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

CGGAGCTATC	CTTGTAGTAG	CTTCAACTGA	CGGACCAATG	CCACAAACTC	GTGAGCACAT	60
CCTTCTTTCA	CGTCAGGTTG	GTGTTAAACA	CCTTATCGTC	TTCATGAACA	AAGTTGACTT	120
GGTTGACGAC	GAAGAATTGC	TTGAATTGGT	TGAAATGGAA	ATCCGTGACC	TATTGTCAGA	180
ATACGACTTC	CCAGGTGACG	ATCTTCCAGT	TATCCAAGGT	TCAGCACTTA	AAGCTCTTGA	240
AGGTGACTCT	AAATACGAAG	ACATCGTTAT	GGAATTGATG	AACACAGTTG	ATGAGTATAT	300
CCCAGAACCA	GAACGTGACA	CTGACAAACC	ATTGCTTCTT	CCAGTCGAGG	ACGTATTCTC	360
AATCACTGGA	CGTGGTACAG	TTGCTTCAGG	ACGTATCGAC	CGTGGTATCG	TTAAAGTCAA	420
CGACGAAATC	GAAATCGTTG	GTATCAAAGA	AGAAACTCRA	AAAGCAGTTG	TTACTGGTGT	480
TGAAATGTTC	CGTAAACAAC	TTGACGAAGG	TCTTGCTGGA	GATAACGTAG	GTGTCCTTCT	540
TCGTGGTGTT	CAACGTGATG	AAATCGAACG	TGGACAAGTT	ATCGCTAAAC	CAGGTTCAAT	600
CAACCCACAC	ACTAAATTCA	AAGGTGAAGT	CTACATCCTT	ACTAAAGAAG	AAGGTGGACG	660
TCACACTCCA	TTCTTCAACA	ACTACCGTCC	ACAATTCTAC	TTCCGTACTA	CTGACGTTAC	720
AGGTTCAATC	GAACTTCCAG	CAGGTACTGA	AATGGTAATG	CCTGGTGATA	ACGTGACAAT	780
CGACGTTGAG	TTGATTCACC	CAATCGCCGT	AGAACAA			817

- (2) INFORMATION FOR SEQ ID NO: 146:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 817 base pairs
 - (B) TYPE: nucleic acid

- 134 -

- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus salivarius
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

CGGTGCGATC	CTTGTAGTAG	CATCTACTGA	CGGACCAATG	CCACAAACTC	GTGAGCACAT	60
CCTTCTTTCA	CGTCAGGTTG	GTGTTAAACA	CCTTATCGTC	TTCATGAACA	AAGTTGACTT	120
GGTTGACGAT	GAAGAATTGC	TTGAATTGGT	TGAAATGGAA	ATCCGTGACC	TTCTTTCAGA	180
ATACGATTTC	CCAGGTGATG	ACATTCCAGT	TATCCAAGGT	TCAGCTCTTA	AAGCTCTTGA	240
AGGTGATTCT	AAATACGAAG	ACATCATCAT	GGACTTGATG	AACACTGTTG	ACGAATACAT	300
CCCAGAACCA	GAACGTGACA	CTGACAAACC	ATTGTTGCTT	CCAGTCGAAG	ACGTATTCTC	360
AATCACTGGT	CGTGGTACTG	TTGCTTCAGG	ACGTATCGAC	CGTGGTGTTG	TTCGTGTCAA	420
TGACGAAGTT	GAAATCGTTG	GTCTTAAAGA	AGACATCCAA	AAAGCAGTTG	TTACTGGTGT	480
TGAAATGTTC	CGTAAACAAC	TTGACGRAGG	TATTGCCGGA	GATAACGTCG	GTGTTCTTCT	540
TCGTGGTATC	CAACGTGATG	AAATCGAACG	TGGTCAAGTA	TTGGCTGCAC	CTGGTTCAAT	600
CAACCCACAC	ACTAAATTCA	AAGGTGAAGT	TTACATCCTT	TCTAAAGAAG	AAGGTGGACG	660
TCACACTCCA	TTCTTCAACA	ACTACCGTCC	ACAGTTCTAC	TTCCGTACAA	CTGACGTAAC	720
AGGTTCAATC	GAACTTCCTG	CAGGTACTGA	AATGGTTATG	CCTGGTGATA	ACGTGACTAT	780
CGACGTTGAG	TTGATCCACC	CAATCGCCGT	TGAACAA			817

- (2) INFORMATION FOR SEQ ID NO: 147:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 897 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Agrobacterium tumefaciens
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

AACATGATCA CCGGTGCTGC CGAGATGGAC GGCGCGATCC TGGTTTGCTC GGCTGCCGAC 60
GGCCCGATGC CACAGACCCG CGAGCACATC CTGCTTGCCC GTCAGGTGGG CGTTCCGGCC 120

ATCGTCGTGT	TCCTCAACAA	GGTCGACCAG	GTTGACGACG	CCGAGCTTCT	CGAGCTCGTC	180
GAGCTTGAAG	TTCGCGAACT	TCTGTCGTCC	TACGACTTCC	CGGGCGACGA	TATCCCGATC	240
ATCAAGGGTT	CGGCACTTGC	TGCTCTTGAA	GATTCTGACA	AGAAGATCGG	TGAAGACGCG	300
ATCCGCGAGC	TGATGGCTGC	TGTCGACGCC	TACATCCCGA	CGCCTGAGCG	TCCGATCGAC	360
CAGCCGTTCC	TGATGCCGAT	CGAAGACGTG	TTCTCGATCT	CGGGTCGTGG	TACGGTTGTG	420
ACGGGTCGCG	TTGAGCGCGG	TATCGTCAAG	GTTGGTGAAG	AAGTCGAAAT	CGTCGGCATC	480
CGTCCGACCT	CGAAGACGAC	TGTTACCGGC	GTTGAAATGT	TCCGCAAGCT	GCTCGACCAG	540
GGCCAGGCCG	GCGACAACAT	CGGTGCACTC	GTTCGCGGCG	TTACCCGTGA	CGGCGTCGAG	600
CGTGGTCAGA	TCCTGTGCAA	GCCGGGTTCG	GTCAAGCCGC	ACAAGAAGTT	CATGGCAGAA	660
GCCTACATCC	TGACGAAGGA	AGAAGGCGGC	CGTCATACGC	CGTTCTTCAC	GAACTACCGT	720
CCGCAGTTCT	ACTTCCGTAC	GACTGACGTT	ACCGGTATCG	TTTCGCTTCC	TGAAGGCACG	780
GAAATGGTTA	TGCCTGGCGA	CAACGTCACT	GTTGAAGTCG	AGCTGATCGT	TCCGATCGCG	840
ATGGAAGAAA	AGCTGCGCTT	CGCTATCCGC	GAAGGCGGCC	GTACCGTCGG	CGCCGGC	897

- (2) INFORMATION FOR SEQ ID NO: 148:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 885 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Bacillus subtilis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

ATGATCACTG GTGCTGCGCA AATGGACGGA GCTATCCTTG TAGTATCTGC TGCTGATGGC 60 CCAATGCCAC AAACTCGTGA GCACATCCTT CTTTCTAAAA ACGTTGGTGT ACCATACATC 120 GTTGTATTCT TAAACAAATG CGACATGGTA GACGACGAAG AGCTTCTTGA ACTAGTTGAA 180 ATGGAAGTTC GCGATCTTCT TAGCGAATAC GACTTCCCTG GTGATGATGT ACCAGTTGTT 240 300 AAAGGTTCTG CTCTTAAAGC TCTTGAAGGA GACGCTGAGT GGGAAGCTAA AATCTTCGAA CTTATGGATG CGGTTGATGA GTACATCCCA ACTCCAGAAC GCGACACTGA AAAACCATTC 360 ATGATGCCAG TTGAGGACGT ATTCTCAATC ACTGGTCGTG GTACAGTTGC TACTGGCCGT 420 GTAGAACGCG GACAAGTTAA AGTCGGTGAC GAAGTTGAAA TCATCGGTCT TCAAGAAGAG 480 - 136 -

AACAAGAAAA CAACTGTTAC AGGTGTTGAA ATGTTCCGTA AGCTTCTTGA TTACGCTGAA 540
GCTGGTGACA ACATTGGTGC CCTTCTTCGC GGTGTATCTC GTGAAGAAAT CCAACGTGGT 600
CAAGTACTTG CTAAACCAGG TACAATCACT CCACACAGCA AATTCAAAGC TGAAGTTTAC 660
GTTCTTTCTA AAGAAGAGGG TGGACGTCAT ACTCCATTCT TCTCTAACTA CCGTCCTCAG 720
TTCTACTTCC GTACAACTGA CGTAACTGGT ATCATCCATC TTCCAGAAGG CGTAGAAATG 780
GTTATGCCTG GAGATAACAC TGAAATGAAC GTTGAACTTA TTTCTACAAT CGCTATCGAA 840
GAAGGAACTC GTTTCTCTAT TCGTGAAGGC GGACGTACTG TTGGT 885

- (2) INFORMATION FOR SEQ ID NO: 149:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 882 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Bacteroides fragilis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

ATGGTTACTG GTGCTGCTCA GATGGACGGT GCTATCATTG TAGTTGCTGC TACTGATGGT 60 CCGATGCCTC AGACTCGTGA GCACATCCTT TTGGCTCGTC AGGTAAACGT TCCGAAGCTG 120 GTTGTATTCA TGAACAAGTG CGATATGGTT GAAGATGCTG AGATGTTGGA ACTTGTTGAA 180 ATGGAAATGA GAGAATTGCT TTCATTCTAT GATTTCGACG GTGACAATAC TCCGATCATT 240 CAGGGTTCTG CTCTTGGTGC ATTGAACGGC GTAGAAAAAT GGGAAGACAA AGTAATGGAA 300 CTGATGGAAG CTGTTGATAC TTGGATTCCA CTGCCTCCGC GCGATGTTGA TAAACCTTTC 360 TTGATGCCGG TAGAAGACGT GTTCTCTATC ACAGGTCGTG GTACTGTAGC TACAGGTCGT 420 ATCGAAACTG GTGTTATCCA TGTAGGTGAT GAAATCGAAA TCCTCGGTTT GGGTGAAGAT 480 AAGAAATCAG TTGTAACAGG TGTTGAAATG TTCCGCAAAC TTCTGGATCA GGGTGAAGCT 540 GGTGACAACG TAGGTCTGTT GCTTCGTGGT GTTGACAAGA ACGAAATCAA ACGTGGTATG 600 GTTCTTTGTA AACCGGGTCA GATTAAACCT CACTCTAAAT TCAAAGCAGA GGTTTATATC 660 CTGAAGAAG AAGAAGGTGG TCGTCACACT CCATTCCATA ACAAATATCG TCCTCAGTTC 720 TACCTGCGTA CTATGGACTG TACAGGTGAA ATCACTCTTC CGGAAGGAAC TGAAATGGTA 780 ATGCCGGGTG ATAACGTAAC TATCACTGTA GAGTTGATCT ATCCGGTTGC ACTGAACATC 840

- 137 -

GGTCTTCGTT TCGCTATCCG CGAAGGTGGA CGTACAGTAG GT

882

- (2) INFORMATION FOR SEQ ID NO: 150:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 888 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Borrelia burgdorferi
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

AATATGATTA CAGGAGCAGC TCAAATGGAT GCAGCGATAC TTTTAGTTGC TGCTGATAGT 60 GGTGCTGAGC CTCAAACAAA AGAGCATTTG CTTCTTGCTC AAAGAATGGG AATAAAGAAA 120 ATAATAGTTT TTTTAAATAA ATTGGACTTA GCAGATCCTG AACTTGTTGA GCTTGTTGAA 180 GTTGAAGTTT TAGAACTTGT TGAAAAATAT GGCTTTTCAG CTGATACTCC AATAATCAAA 240 GGTTCAGCTT TTGGGGCTAT GTCAAATCCA GAAGATCCTG AATCTACAAA ATGCGTTAAA 300 GAACTTCTTG AATCTATGGA TAATTATTTT GATCTTCCAG AAAGAGATAT TGACAAGCCA 360 TTTTTGCTTG CTGTTGAAGA TGTATTTCT ATTTCAGGAA GAGGCACTGT TGCTACTGGG 420 CGTATTGAAA GAGGTATTAT TAAAGTTGGT CAAGAAGTTG AAATAGTTGG AATTAAAGAA 480 ACCAGAAAAA CTACTGTTAC TGGTGTTGAA ATGTTCCAGA AAATTCTTGA GCAAGGTCAA 540 GCAGGGGATA ATGTTGGTCT TCTTTTGAGA GGCGTTGATA AAAAAGACAT TGAGAGGGGG 600 CAAGTTTTGT CAGCTCCAGG TACAATTACT CCACACAAGA AATTTAAAGC TTCAATTTAT 660 TGTTTGACTA AAGAAGAAGG CGGTAGGCAC AAGCCATTTT TCCCAGGGTA TAGACCACAG 720 TTCTTTTTA GAACAACCGA TGTTACTGGA GTTGTTGCTT TAGAGGGCAA AGAAATGGTT 780 ATGCCTGGTG ATAATGTTGA TATTATTGTT GAGCTGATCT CTTCAATAGC TATGGATAAG 840 AATGTAGAAT TTGCTGTTCG AGAAGGTGGA AGAACCGTTG CTTCAGGA 888

- (2) INFORMATION FOR SEQ ID NO: 151:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 894 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

- 138 -

(vi)	ORIG	LIAN	SOURCE	3:	
	(A)	ORGA	MISM:	Brevibacterium	linens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

AACATGATCA	CCGGTGCCGC	TCAGATGGAC	GGTGCGATCC	TCGTCGTCGC	CGCTACCGAC	60
GGACCGATGC	CCCAGACCCG	TGAGCACGTG	CTGCTCGCGC	GTCAGGTCGG	CGTTCCCTAC	120
ATCGTCGTGG	CTCTGAACAA	GTCCGACATG	GTCGATGACG	AGGAGCTCCT	CGAGCTCGTC	180
GAATTCGAGG	TCCGCGACCT	GCTCTCGAGC	CAGGACTTCG	ACGGAGACAA	CGCTCCGGTC	240
ATTCCGGTGT	CCGCTCTCAA	GGCGCTGGAA	GGCGACGAGA	AGTGGGTCAA	GAGCGTTCAG	300
GATCTCATGG	CTGCCGTCGA	TGACAACGTT	CCGGAGCCGG	AGCGCGATGT	CGACAAGCCG	360
TTCCTCATGC	CCGTCGAGGA	CGTCTTCACG	ATCACCGGTC	GTGGAACCGT	CGTCACCGGT	420
CGTGTCGAGC	GCGGCGTGCT	CCTGCCTAAC	GACGAAATCG	AAATCGTCGG	CATCAAGGAG	480
AAGTCGTCCA	AGACGACTGT	CACCGCTATC	GAGATGTTCC	GCAAGACCCT	GCCGGATGCC	540
CGTGCAGGTG	AGAACGTCGG	TCTGCTCCTC	CGCGGCACCA	AGCGCGAGGA	TGTTGAGCGC	600
GGTCAGGTCA	TCGTGAAGCC	GGGTTCGATC	ACCCCGCACA	CCAAGTTCGA	GGCTCAGGTC	660
TACATCCTGA	GCAAGGACGA	GGGCGGACGT	CACAACCCGT	TCTACTCGAA	CTACCGTCCG	720
CAGTTCTACT	TCCGGACCAC	GGACGTCACC	GGTGTCATCA	CGCTGCCCGA	GGGCACCGAG	780
ATGGTCATGC	CCGGCGACAA	CACCGATATG	TCGGTCGAGC	TCATCCAGCC	GATCGCTATG	840
GAGGACCGCC	TCCGCTTCGC	AATCCGCGAA	GGTGGCCGCA	CCGTCGGCGC	CGGT	894

- (2) INFORMATION FOR SEQ ID NO: 152:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 888 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Burkholderia cepacia
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

ATGATCACGG GCGCAGCGCA GATGGACGGC GCGATCCTGG TTTGCTCGGC AGCAGACGGC 60

CCGATGCCGC AAACGCGTGA GCACATCCTG CTGGCGCGTC AGGTTGGTGT TCCGTACATC 120

ATCGTGTTCC TGAACAAGTG CGACAGTGTG GACGACGCTG AACTGCTCGA GCTGGTCGAG 180

ATGGAAGTTC	GCGAACTCCT	GTCGAAGTAC	GACTTCCCGG	GCGACGACAC	GCCGATCGTG	240
AAGGGTTCGG	CCAAGCTGGC	GCTGGAAGGC	GACACGGGCG	AGCTGGGCGA	AGTGGCGATC	300
ATGAGCCTGG	CAGACGCGCT	GGACACGTAC	ATCCCGACGC	CGGAGCGTGC	AGTTGACGGC	360
GCGTTCCTGA	TGCCGGTGGA	AGACGTGTTC	TCGATCTCGG	GCCGTGGTAC	GGTGGTGACG	420
GGTCGTGTCG	AGCGCGGCAT	CGTGAAGGTC	GGCGAAGAAA	TCGAAATCGT	CGGTATCAAG	480
CCGACGGTGA	AGACGACCTG	CACGGGCGTT	GAAATGTTCC	GCAAGCTGCT	GGACCAAGGT	540
CAGGCAGGCG	ACAACGTCGG	TATCCTGCTG	CGCGGCACGA	AGCGTGAAGA	CGTGGAGCGT	600
GGCCAGGTTC	TGGCGAAGCC	GGGTTCGATC	ACGCCGCACA	CGCACTTCAC	GGCTGAAGTG	660
TACGTGCTGA	GCAAGGACGA	AGGCGGCCGT	CACACGCCGT	TCTTCAACAA	CTACCGTCCG	720
CAGTTCTACT	TCCGTACGAC	GGACGTGACG	GGCTCGATCG	AGCTGCCGAA	GGACAAGGAA	780
ATGGTGATGC	CGGGCGACAA	CGTGTCGATC	ACGGTGAAGC	TGATTGCTCC	GATCGCGATG	840
GAAGAAGGTC	TGCGCTTCGC	AATCCGTGAA	GGCGGCCGTA	CGGTCGGC		888

- (2) INFORMATION FOR SEQ ID NO: 153:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Chlamydia trachomatis
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

AACATGATCA	CCGGTGCGGC	TCAAATGGAC	GGGGCTATTC	TAGTAGTTTC	TGCAACAGAC	60
GGAGCTATGC	CTCAAACTAA	AGAGCATATT	CTTTTGGCAA	GACAAGTTGG	GGTTCCTTAC	120
ATCGTTGTTT	TTCTCAATAA	AATTGACATG	ATTTCCGAAG	AAGACGCTGA	ATTGGTCGAC	180
TTGGTTGAGA	TGGAGTTGGC	TGAGCTTCTT	GAAGAGAAAG	GATACAAAGG	GTGTCCAATC	240
ATCAGAGGTT	CTGCTCTGAA	AGCTTTGGAA	GGAGATGCTG	CATACATAGA	GAAAGTTCGA	300
GAGCTAATGC	AAGCCGTCGA	TGATAATATC	CCTACTCCAG	AAAGAGAAAT	TGACAAGCCT	360
TTCTTAATGC	CTATTGAGGA	CGTGTTCTCT	ATCTCCGGAC	GAGGAACTGT	AGTAACTGGA	420
CGTATTGAGC	GTGGAATTGT	TAAAGTTTCC	GATAAAGTTC	AGTTGGTCGG	TCTTAGAGAT	480
ACTAAAGAAA	CGATTGTTAC	TGGGGTTGAA	ATGTTCAGAA	AAGAACTCCC	AGAAGGTCGT	540

GCAGGAGAGA ACGTTGGATT GCTCCTCAGA GGTATTGGTA AGAACGATGT GGAAAGAGGA 600
ATGGTTGTTT GCTTGCCAAA CAGTGTTAAA CCTCATACAC AGTTTAAGTG TGCTGTTTAC 660
GTTCTGCAAA AAGAAGAAGG TGGACGACAT AAGCCTTTCT TCACAGGATA TAGACCTCAA 720
TTCTTCTTCC GTACAACAGA CGTTACAGGT GTGGTAACTC TGCCTGAGGG AGTTGAGATG 780
GTCATGCCTG GGGATAACGT TGAGTTTGAA GTGCAATTGA TTAGCCCTGT GGCTTTAGAA 840
GAAGGTATGA GATTTGCGAT TCGTGAAGGT GGTCGTACAA TCGGTGCTGG A 891

(2) INFORMATION FOR SEQ ID NO: 154:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Escherichia coli
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

AACATGATCA CCGGTGCTGC GCAGATGGAC GGCGCGATCC TGGTAGTTGC TGCGACTGAC 60 GGCCCGATGC CGCAGACTCG TGAGCACATC CTGCTGGGTC GTCAGGTAGG CGTTCCGTAC 120 ATCATCGTGT TCCTGAACAA ATGCGACATG GTTGATGACG AAGAGCTGCT GGAACTGGTT 180 GAAATGGAAG TTCGTGAACT TCTGTCTCAG TACGACTTCC CGGGCGACGA CACTCCGATC 240 GTTCGTGGTT CTGCTCTGAA AGCGCTGGAA GGCGACGCAG AGTGGGAAGC GAAAATCCTG 300 GAACTGGCTG GCTTCCTGGA TTCTTACATT CCGGAACCAG AGCGTGCGAT TGACAAGCCG 360 TTCCTGCTGC CGATCGAAGA CGTATTCTCC ATCTCCGGTC GTGGTACCGT TGTTACCGGT 420 CGTGTAGAAC GCGGTATCAT CAAAGTTGGT GAAGAAGTTG AAATCGTTGG TATCAAAGAG 480 ACTCAGAAGT CTACCTGTAC TGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGCCGT 540 GCTGGTGAGA ACGTAGGTGT TCTGCTGCGT GGTATCAAAC GTGAAGAAAT CGAACGTGGT 600 CAGGTACTGG CTAAGCCGGG CACCATCAAG CCGCACACCA AGTTCGAATC TGAAGTGTAC 660 ATTCTGTCCA AAGATGAAGG CGGCCGTCAT ACTCCGTTCT TCAAAGGCTA CCGTCCGCAG 720 TTCTACTTCC GTACTACTGA CGTGACTGGT ACCATCGAAC TGCCGGAAGG CGTAGAGATG 780 GTAATGCCGG GCGACAACAT CAAAATGGTT GTTACCCTGA TCCACCCGAT CGCGATGGAC 840 GACGGTCTGC GTTTCGCAAT CCGTGAAGGC GGCCGTACCG TTGGCGCGGG C 891

- (2) INFORMATION FOR SEQ ID NO: 155:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Fibrobacter succinogenes
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

AACATGGTGA CTGGTGCTGC TCAGATGGAC GGCGCTATCC TCGTTGTTGC CGCTACTGAC 60 GGTCCGATGC CGCAGACTCG CGAACACATC CTTCTCGCTC ACCAGGTTGG CGTGCCGAAG 120 ATCGTCGTGT TCATGAACAA GTGCGACATG GTTGACGATG CTGAAATTCT CGACCTCGTC 180 GAAATGGAAG TTCGCGAACT CCTCTCCAAG TATGACTTCG ACGGTGACAA CACCCCGATC 240 ATCCGTGGTT CCGCTCTCAA GGCCCTCGAA GGCGATCCGG AATACCAGGA CAAGGTCATG 300 GAACTCATGA ACGCTTGCGA CGAATACATC CCGCTCCCGC AGCGCGATAC CGACAAGCCG 360 TTCCTCATGC CGATCGAAGA CGTGTTCACG ATTACTGGCC GCGGCACTGT CGCTACTGGC 420 CGTATCGAAC GCGGTGTCGT TCGCTTGAAC GACAAGGTTG AACGTATCGG TCTCGGTGAA 480 ACCACCGAAT ACGTCATCAC CGGTGTTGAA ATGTTCCGTA AGCTCCTCGA CGACGCTCAG 540 GCAGGTGACA ACGTTGGTCT CCTCCTCCGT GGTGCTGAAA AGAAGGACAT CGTCCGTGGC 600 ATGGTTCTCG CAGCTCCGAA GTCTGTCACT CCGCACACCG AATTTAAGGC TGAAATCTAC 660 GTTCTCACGA AGGACGAAGG TGGCCGTCAC ACGCCGTTCA TGAATGGCTA CCGTCCGCAG 720 TTCTACTTCC GCACCACCGA CGTTACTGGT ACGATCCAGC TCCCGGAAGG TGTCGAAATG 780 GTTACTCCGG GTGACACGGT CACGATCCAC GTGAACCTCA TCGCTCCGAT CGCTATGGAA 840 AAGCAGCTCC GCTTCGCTAT CCGTGAAGGT GGACGTACTG TTGGTGCTGG C 891

- (2) INFORMATION FOR SEQ ID NO: 156:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 894 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:

- 142 -

(A) ORGANISM: Flavobacterium ferrugineum

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

AACATGATCA	CCGGTGCTGC	CCAGATGGAC	GGTGCTATCT	TAGTTGTGGC	TGCATCAGAC	60
GGTCCTATGC	CTCAAACAAA	AGAACACATC	CTGCTTGCTG	CCCAGGTAGG	TGTACCTAAA	120
ATGGTTGTGT	TTCTGAATAA	AGTTGACCTC	GTTGACGACG	AAGAGCTCCT	GGAGCTGGTT	180
GAGATCGAGG	TTCGCGAAGA	ACTGACTAAA	CGCGGTTTCG	ACGGCGACAA	CACTCCAATC	240
ATCAAAGGTT	CCGCTACAGG	CGCCCTCGCT	ĢĢTGAAGAAA	AGTGGGTTAA	AGAAATTGAA	300
AACCTGATGG	ACGCTGTTGA	CAGCTACATC	CCACTGCCTC	CTCGTCCGGT	TGATCTGCCG	360
TTCCTGATGA	GCGTAGAGGA	CGTATTCTCT	ATCACTGGTC	GTGGTACTGT	TGCTACCGGT	420
CGTATCGAGC	GTGGCCGTAT	CAAAGTTGGT	GAGCCTGTTG	AGATCGTAGG	TCTGCAGGAG	480
TCTCCCCTGA	ACTCTACCGT	TACAGGTGTT	GAGATGTTCC	GCAAACTCCT	CGACGAAGGT	540
GAAGCTGGTG	ATAACGCCGG	TCTCCTCCTC	CGTGGTGTTG	AAAAAACACA	GATCCGTCGC	600
GGTATGGTAA	TCGTTAAACC	CGGTTCCATC	ACTCCGCACA	CGGACTTCAA	AGGCGAAGTT	660
TACGTACTGA	GCAAAGACGA	AGGTGGCCGT	CACACTCCAT	TCTTCAACAA	ATACCGTCCT	720
CAATTCTACT	TCCGTACAAC	TGACGTTACA	GGTGAAGTAG	AACTGAACGC	AGGAACAGAA	780
ATGGTTATGC	CTGGTGATAA	CACCAACCTG	ACCGTTAAAC	TGATCCAACC	GATCGCTATG	840
GAAAAAGGTC	TGAAATTCGC	GATCCGCGAA	GGTGGCCGTA	CCGTAGGTGC	AGGA	894

- (2) INFORMATION FOR SEQ ID NO: 157:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Haemophilus influenzae
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

AATATGATTA CTGGTGCGGC ACAAATGGAT GGTGCTATTT TAGTAGTAGC AGCAACAGAT 60

GGTCCTATGC CACAAACTCG TGAACACATC TTATTAGGTC GCCAAGTAGG TGTTCCATAC 120

ATCATCGTAT TCTTAAACAA ATGCGACATG GTAGATGACG AAGAGTTATT AGAATTAGTC 180

GAAATGGAAG TTCGTGAACT TCTATCTCAA TATGACTTCC CAGGTGACGA TACACCAATC 240

- 143 -

GTACGTGGTT CAGCATTACA AGCGTTAAAC GGCGTAGCAG AATGGGAAGA AAAAATCCTT 300 GAGTTAGCAA ACCACTTAGA TACTTACATC CCAGAACCAG AACGTGCGAT TGACCAACCG 360 TTCCTTCTTC CAATCGAAGA TGTGTTCTCA ATCTCAGGTC GTGGTACTGT AGTAACAGGT 420 CGTGTAGAAC GAGGTATTAT CCGTACAGGT GATGAAGTAG AAATCGTCGG TATCAAAGAT 480 ACAGCGAAAA CTACTGTAAC GGGTGTTGAA ATGTTCCGTA AATTACTTGA CGAAGGTCGT 540 GCAGGTGAAA ACATCGGTGC ATTATTACGT GGTACCAAAC GTGAAGAAAT CGAACGTGGT 600 CAAGTATTAG CGAAACCAGG TTCAATCACA CCACACACTG ACTTCGAATC AGAAGTGTAC 660 GTATTATCAA AAGATGAAGG TGGTCGTCAT ACTCCATTCT TCAAAGGTTA CCGTCCACAA 720 TTCTATTTCC GTACAACAGA CGTGACTGGT ACAATCGAAT TACCAGAAGG CGTGGAAATG 780 GTAATGCCAG GCGATAACAT CAAGATGACA GTAAGCTTAA TCCACCCAAT TGCGATGGAT 840 CAAGGTTTAC GTTTCGCAAT CCGTGAAGGT GGCCGTACAG TAGGTGCAGG C 891

- (2) INFORMATION FOR SEQ ID NO: 158:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 906 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Helicobacter pylori
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

AACATGATCA CCGGTGCGGC GCAAATGGAC GGAGCGATTT TGGTTGTTTC TGCAGCTGAT 60 GGCCCTATGC CTCAAACTAG GGAGCATATC TTATTGTCTC GTCAAGTAGG CGTGCCTCAC 120 ATCGTTGTTT TCTTAAACAA ACAAGACATG GTAGATGACC AAGAATTGTT AGAACTTGTA 180 GAAATGGAAG TGCGCGAATT GTTGAGCGCG TATGAATTTC CTGGCGATGA CACTCCTATC 240 GTAGCGGGTT CAGCTTTAAG AGCTTTAGAA GAAGCAAAGG CTGGTAATGT GGGTGAATGG 300 GGTGAAAAAG TGCTTAAACT TATGGCTGAA GTGGATGCCT ATATCCCTAC TCCAGAAAGA 360 GACACTGAAA AAACTTTCTT GATGCCGGTT GAAGATGTGT TCTCTATTGC GGGTAGAGGG 420 ACTGTGGTTA CAGGTAGGAT TGAAAGAGGC GTGGTGAAAG TAGGCGATGA AGTGGAAATC 480 GTTGGTATCA GACCTACACA AAAAACGACT GTAACCGGTG TAGAAATGTT TAGGAAAGAG 540 TTGGAAAAG GTGAAGCCGG CGATAATGTG GGCGTGCTTT TGAGAGGAAC TAAAAAAGAA 600

- 144 -

GAAGTGGAAC GCGGTATGGT TCTATGCAAA CCAGGTTCTA TCACTCCGCA CAAGAAATTT 660
GAGGGAGAAA TTTATGTCCT TTCTAAAGAA GAAGGCGGGA GACACACTCC ATTCTTCACC 720
AATTACCGCC CGCAATTCTA TGTGCGCACA ACTGATGTGA CTGGCTCTAT CACCCTTCCT 780
GAAGGCGTAG AAATGGTTAT GCCTGGCGAT AATGTGAAAA TCACTGTAGA GTTGATTAGC 840
CCTGTTGCGT TAGAGTTGGG AACTAAATTT GCGATTCGTG AAGGCGGTAG GACCGTTGGT 900
GCTGGT

(2) INFORMATION FOR SEQ ID NO: 159:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Micrococcus luteus
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

AACATGATCA CCGGCGCCGC TCAGATGGAC GGCGCGATCC TCGTGGTCGC CGCTACCGAC 60 GGCCCGATGG CCCAGACCCG TGAGCACGTG CTCCTGGCCC GCCAGGTCGG CGTGCCGGCC 120 CTGCTCGTGG CCCTGAACAA GTCGGACATG GTGGAGGACG AGGAGCTCCT CGAGCGTGTC 180 GAGATGGAGG TCCGGCAGCT GCTGTCCTCC AGGAGCTTCG ACGTCGACGA GGCCCCGGTC 240 ATCCGCACCT CCGCTCTGAA GGCCCTCGAG GGCGACCCCC AGTGGGTCAA GTCCGTCGAG 300 GACCTCATGG ATGCCGTGGA CGAGTACATC CCGGACCCGG TGCGCGACAA GGACAAGCCG 360 TTCCTGATGC CGATCGAGGA CGTCTTCACG ATCACCGGCC GTGGCACCGT GGTGACCGGT 420 CGCGCCGAGC GCGGCACCCT GAAGATCAAC TCCGAGGTCG AGATCGTCGG CATCCGCGAC 480 GTGCAGAAGA CCACTGTCAC CGGCATCGAG ATGTTCCACA AGCAGCTCGA CGAGGCCTGG 540 GCCGGCGAGA ACTGCGGTCT GCTCGTGCGC GGTCTGAAGC GCGACGACGT CGAGCGCGGC 600 CAGGTGCTGG TGGAGCCGGG CTCCATCACC CCGCACACCA ACTTCGAGGC GAACGTCTAC 660 ATCCTGTCCA AGGACGAGGG TGGGCGTCAC ACCCCGTTCT ACTCGAACTA CCGCGCGCAG 720 TTCTACTTCC GCACCACCGA CGTCACCGGC GTCATCACGC TGCCCGAGGG CACCGAGATG 780 GTCATGCCCG GCGACACCAC CGAGATGTCG GTCGAGCTCA TCCAGCCGAT CGCCATGGAG 840 GAGGGCCTCG GCTTCGCCAT CCGCGAGGGT GGCCGCACCG TGGGCTCCGG C 891

- 145 -

(2) INFORMATION FOR SEQ ID NO: 160:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Mycobacterium tuberculosis
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

AACATGATCA CCGGCGCCGC GCAGATGGAC GGTGCGATCC TGGTGGTCGC CGCCACCGAC 60 GGCCCGATGC CCCAGACCCG CGAGCACGTT CTGCTGGCGC GTCAAGTGGG TGTGCCCTAC 120 ATCCTGGTAG CGCTGAACAA GGCCGACGCA GTGGACGACG AGGAGCTGCT CGAACTCGTC 180 GAGATGGAGG TCCGCGAGCT GCTGGCTGCC CAGGAATTCG ACGAGGACGC CCCGGTTGTG 240 CGGGTCTCGG CGCTCAAGGC GCTCGAGGGT GACGCGAAGT GGGTTGCCTC TGTCGAGGAA 300 CTGATGAACG CGGTCGACGA GTCGATTCCG GACCCGGTCC GCGAGACCGA CAAGCCGTTC 360 CTGATGCCGG TCGAGGACGT CTTCACCATT ACCGGCCGCG GAACCGTGGT CACCGGACGT 420 GTGGAGCGCG GCGTGATCAA CGTGAACGAG GAAGTTGAGA TCGTCGGCAT TCGCCCATCG 480 ACCACCAAGA CCACCGTCAC CGGTGTGGAG ATGTTCCGCA AGCTGCTCGA CCAGGGCCAG 540 GCGGCCGACA ACGTTGGTTT GCTGCTGCGG GGCGTCAAGC GCGAGGACGT CGAGCGTGGC 600 CAGGTTGTCA CCAAGCCCGG CACCACCACG CCGCACACCG AGTTCGAAGG CCAGGTCTAC 660 ATCCTGTCCA AGGACGAGGG CGGCCGGCAC ACGCCGTTCT TCAACAACTA CCGTCCGCAG 720 TTCTACTTCC GCACCACCGA CGTGACCGGT GTGGTGACAC TGCCGGAGGG CACCGAGATG 780 GTGATGCCCG GTGACACAC CAACATCTCG GTGAAGTTGA TCCAGCCCGT CGCCATGGAC 840 GAAGGTCTGC GTTTCGCGAT CCGCGAGGGT GGCCGCACCG TGGGCGCCGG C 891

- (2) INFORMATION FOR SEQ ID NO: 161:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:

- 146 -

(A) ORGANISM: Mycoplasma genitalium

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

AATATGATCA	CAGGTGCTGC	ACAAATGGAT	GGAGCTATTC	TAGTTGTTTC	AGCAACTGAT	60
AGTGTGATGC	CCCAAACCCG	CGAGCACATC	TTACTTGCCC	GCCAAGTAGG	GGTTCCTAAA	120
ATGGTAGTTT	TTCTAAACAA	GTGTGATATT	GCTAGTGATG	AAGAGGTACA	AGAACTTGTT	180
GCTGAAGAAG	TACGTGATCT	GTTAACTTCC	TATGGTTTTG	ATGGTAAGAA	CACTCCTATT	240
ATTTATGGCT	CAGCTTTAAA	AGCATTGGAA	GGTGATCCAA	AGTGGGAGGC	TAAGATCCAT	300
GATTTGATTA	AAGCAGTTGA	TGAATGGATT	CCAACTCCTA	CACGTGAAGT	AGATAAACCT	360
TTCTTATTAG	CAATTGAAGA	TACGATGACC	ATTACTGGTA	GAGGTACAGT	TGTTACAGGA	420
AGAGTTGAAA	GAGGTGAACT	CAAAGTAGGT	CAAGAAGTTG	AAATTGTTGG	TTTAAAACCA	480
ATTAGAAAAG	CAGTTGTTAC	TGGAATTGAA	ATGTTCAAAA	AGGAACTTGA	TTCAGCAATG	540
GCTGGTGACA	ATGCTGGGGT	ATTATTACGT	GGTGTTGAAC	GTAAAGAAGT	TGAAAGAGGT	600
CAAGTTTTAG	CAAAACCAGG	CTCTATTAAA	CCGCACAAGA	AATTTAAAGC	TGAGATCTAT	660
GCTTTAAAGA	AAGAAGAAGG	TGGTAGACAC	ACTGGTTTTT	TAAACGGTTA	CCGTCCTCAA	720
TTCTATTTCC	GTACCACTGA	TGTAACTGGT	TCTATTGCTT	TAGCTGAAAA	TACTGAAATG	.780
GTTCTACCTG	GTGATAATGC	TTCTATTACT	GTTGAGTTAA	TTGCTCCTAT	CGCTTGTGAA	840
AAAGGTAGTA	AGTTCTCAAT	TCGTGAAGGT	GGTAGAACTG	TAGGGGCAGG	C	891

(2) INFORMATION FOR SEQ ID NO: 162:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Neisseria gonorrheae
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

AACATGATTA CCGGCGCCGC ACAAATGGAC GGTGCAATCC TGGTATGTTC TGCTGCCGAC 60

GGCCCTATGC CGCAAACCCG CGAACACATC CTGCTGGCCC GTCAAGTAGG CGTACCTTAC 120

ATCATCGTGT TCATGAACAA ATGCGACATG GTCGACGATG CCGAGCTGTT CCAACTGGTT 180

GAAATGGAAA TCCGCGACCT GCTGTCCAGC TACGACTTCC CCGGCGACGA CTGCCCGATC 240

- 1**47** -

GTACAAGGTT	CCGCACTGAA	AGCCTTGGAA	GGCGATGCCG	CTTACGAAGA	AAAAATCTTC	300
GAACTGGCTA	CCGCATTGGA	CAGATACATC	CCGACTCCCG	AGCGTGCCGT	GGACAAACCA	360
TTCCTGCTGC	CTATCGAAGA	CGTGTTCTCC	ATTTCCGGCC	GCGGTACCGT	AGTCACCGGC	420
CGTGTAGAGC	GAGGTATCAT	CCACGTTGGT	GACGAGATTG	AAATCGTCGG	TCTGAAAGAA	480
ACCCAAAAAA	CCACCTGTAC	CGGCGTTGAA	ATGTTCCGCA	AACTGCTGGA	CGAAGGTCAG	540
GCGGGCGACA	ACGTAGGCGT	ATTGCTGCGC	GGTACCAAAC	GTGAAGACGT	AGAACGCGGT	600
CAGGTATTGG	CCAAACGGGG	TACTATCACT	CCTCACACCA	AGTTCAAAGC	AGAAGTGTAC	660
GTATTGAGCA	AAGAAGAGGG	CGGCCCCCAT	ACCCCGTTTT	TCGCCAACTA	CCGTCCCCAA	720
TTCTACTTCC	GTACCACTGA	CGTAACCGGC	ACGATTACTT	TGGAAAAAGG	TGTGGAAATG	780
GTAATGCCGG	GTGAGAACGT	AACCATTACT	GTAGAACTGA	TTGCGCCTAT	CGCTATGGAA	840
GAAGGTCTGC	GCTTTGCGAT	TCGCGAAGGC	GGCCGTACCG	TGGGTGCCGG	С	891

- (2) INFORMATION FOR SEQ ID NO: 163:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Rickettsia prowazekii
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

AATATGATAA	CTGGTGCCGC	TCAGATGGAT	GGTGCTATAT	TAGTAGTTTC	TGCTGCTGAT	60
GGTCCTATGC	CTCAAACTAG	AGAACATATA	TTACTGGCAA	AACAGGTAGG	TGTACCTGCT	120
ATGGTAGTAT	TTTTGAATAA	AGTAGATATG	GTAGATGATC	CTGACCTATT	AGAATTAGTT	180
GAGATGGAAG	TAAGAGAATT	ATTATCAAAA	TATGGTTTCC	CTGGTAATGA	AATACCTATT	240
ATTAAAGGTT	CTGCACTTCA	AGCTTTAGAA	GGAAAACCTG	AAGGTGAAAA	AGCTATTAAT	300
GAGTTAATGA	ATGCAGTAGA	TACGTATATA	CCTCAGCCTA	TAGAGCTACA	AGATAAACCT	360
TTTTTAATGC	CAATAGAGGA	TGTATTTTCT	ATTTCAGGCA	GAGGTACCGT	TGTAACTGGT	420
AGAGTGGAGT	CAGGCATAAT	TAAGGTGGGT	GAAGAAATTG	AAATAGTAGG	TCTAAAAAAT	480
ACGCAAAAA	CGACTTGTAC	AGGTGTAGAA	ATGTTCAGAA	AATTACTTGA	TGAAGGACAA	540
TCTGGAGATA	ATGTCGGTAT	ATTACTACGT	GGTACAAAAA	GAGAAGAAGT	AGAAAGAGGA	600

- 148 -

CAAGTACTTG CAAAACCTGG GAGCATAAAA CCGCATGATA AATTTGAAGC TGAAGTGTAT 660
GTGCTTAGTA AAGAGGAAGG TGGACGTCAT ACCCCATTTA CTAATGATTA TCGCCCACAG 720
TTCTATTTTA GAACAACAGA TGTTACCGGC ACAATAAAAT TGCCTTCTGA TAAGCAGATG 780
GTTATGCCTG GAGATAATGC TACTTTTTCA GTAGAATTAA TTAAGCCGAT TGCTATGCAA 840
GAAGGGTTAA AATTCTCTAT ACGTGAAGGT GGTAGAACAG TAGGAGCCGG T 891

(2) INFORMATION FOR SEQ ID NO: 164:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 891 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Salmonella typhimurium
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

AACATGATCA CCGGTGCTGC TCAGATGGAC GGCGCGATCC TGGTTGTTGC TGCGACTGAC 60 GGCCCGATGC CGCAGACCCG TGAGCACATC CTGCTGGGTC GTCAGGTAGG CGTTCCGTAC 120 ATCATCGTGT TCCTGAACAA ATGCGACATG GTTGATGACG AAGAGCTGCT GGAACTGGTT 180 GAGATGGAAG TTCGCGAACT GCTGTCTCAG TACGACTTCC CGGGCGACGA CACTCCGATC 240 GTTCGTGGTT CTGCTCTGAA AGCGCTGGAA GGCGACGCAG AGTGGGAAGC GAAAATCATC 300 GAACTGGCTG GCTTCCTGGA TTCTTATATT CCGGAACCAG AGCGTGCGAT TGACAAGCCG 360 TTCCTGCTGC CGATCGAAGA CGTATTCTCC ATCTCCGGTC GTGGTACCGT TGTTACCGGT 420 CGTGTAGAGC GCGGTATCAT CAAAGTGGGC GAAGAAGTTG AAATCGTTGG TATCAAAGAG 480 ACTCAGAAGT CTACCTGTAC TGGCGTTGAA ATGTTCCGCA AACTGCTGGA CGAAGGCCGT 540 GCCGGTGAGA ACGTAGGTGT TCTGCTGCGT GGTATCAAAC GTGAAGAAAT CGAACGTGGT 600 CAGGTACTGG CTAAGCCGGG CACCATCAAG CCGCACACCA AGTTCGAATC TGAAGTGTAC 660 ATTCTGTCCA AAGATGAAGG CGGCCGTCAT ACTCCGTTCT TCAAAGGCTA CCGTCCGCAG 720 TTCTACTTCC GTACTACTGA CGTGACTGGT ACCATCGAAC TGCCGGAAGG CGTAGAGATG 780 GTAATGCCGG GCGACAACAT CAAAATGGTT GTTACCCTGA TCCACCCGAT CGCGATGGAC 840 GACGGTCTGC GTTTCGCAAT CCGTGAAGGC GGCCGTACCG TTGGCGCGGG C 891

(2) INFORMATION FOR SEQ ID NO: 165:

- 149 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 881 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Shewanella putida
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

ATGATCACTG GTGCTGCACA GATGGACGGC GCGATTCTGG TAGTCGCTTC AACAGACGGT 60 CCAATGCCAC AGACTCGTGA GCACATCCTG CTTTCTCGTC AGGTTGGCGT ACCATTCATC 120 ATCGTATTCA TGAACAATG TGACATGGTA GATGACGAAG AGCTGTTAGA GCTAGTTGAG 180 ATGGAAGTGC GTGAACTGTT ATCAGAATAC GATTTCCCAG GTGATGACTT ACCGGTAATC 240 CAAGGTTCAG CTCTGAAAGC GCTAGAAGGC GAGCCAGAGT GGGAAGCAAA AATCCTTGAA 300 TTAGCAGCGG CGCTGGATTC TTACATTCCA GAACCACAAC GTGACATCGA TAAGCCGTTC 360 CTACTGCCAA TCGAAGACGT ATTCTCAATT TCAGGCCGTG GTACAGTAGT AACAGGTCGT 420 GTTGAGCGTG GTATTGTACG CGTAGGCGAC GAAGTTGAAA TCGTTGGTGT ACGTGCGACA 480 ACTAAGACAA CGTGTACTGG TGTAGAAATG TTCCGTAAAC TGCTTGACGA AGGTCGTGCA 540 GGTGAGAACT GTGGTATTTT GTTACGTGGT ACTAAGCGTG ATGACGTAGA ACGTGGTCAA 600 GTATTAGCGA AGCCAGGTTC AATCAACCCA CACACTACTT TTGAATCAGA AGTTTACGTA 660 CTGTCAAAAG AAGAAGGTGG TCGTCACACG CCATTCTTCA AAGGCTACCG TCCACAGTTC 720 TACTTCCGTA CAACTGACGT AACCGGTACT ATCGAACTGC CAGAAGGCGT AGAGATGGTA 780 ATGCCAGGCG ATAACATCAA GATGGTAGTG ACACTGATTT GCCCAATCGC GATGGACGAA 840 881 GGTTTACGCT TCGCAATCCG TGAAGGCGGT CGTACAGTGG T

- (2) INFORMATION FOR SEQ ID NO: 166:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 897 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Stigmatella aurantiaca

(xi) SEQUENCE DESC	RIPTION: SEC	ID	NO:	166:
--------------------	--------------	----	-----	------

AACATGATCA	CGGGCGCGGC	GCAGATGGAC	GGAGCGATTC	TGGTGGTGTC	CGCGGCCGAC	60
GGCCCGATGC	CCCAGACGCG	TGAGCACATC	CTGCTGGCCA	GGCAGGTGGG	CGTGCCCTAC	120
ATCGTCGTCT	TCCTGAACAA	GGTGGACATG	CTGGACGATC	CGGAGCTGCG	CGAGCTGGTG	180
GAGATGGAGG	TGCGCGACCT	GCTCAAGAAG	TACGAGTTCC	CGGGCGACAG	CATCCCCATC	240
ATCCCTGGCA	GCGCGCTCAA	GGCGCTGGAG	GGAGACACCA	GCGACATCGG	CGAGGGAGCG	300
ATCCTGAAGC	TGATGGCGGC	GGTGGACGAG	TACATCCCGA	CGCCGCAGCG	TGCGACGGAC	360
AAGCCGTTCC	TGATGCCGGT	GGAAGACGTG	TTCTCCATCG	CAGGCCGAGG	AACGGTGGCG	420
ACGGGCCGAG	TGGAGCGCGG	CAAGATCAAG	GTGGGCGAGG	AAGTGGAGAT	CGTGGGGATC	480
CGTCCGACGC	AGAAGACGGT	CATCACGGGG	GTGGAGATGT	TCCGCAAGCT	GCTGGACGAG	540
GGCATGGCGG	GAGACAACAT	CGGAGCGCTG	CTGCGAGGCC	TGAAGCGCGA	GGACCTGGAG	600
CGTGGGCAGG	TGCTGGCGAA	CTGGGGGAGC	ATCAACCCGC	ACACGAAGTT	CAAGGCGCAG	660
GTGTACGTGC	TGTCGAAGGA	AGAGGGAGGG	CGGCACACGC	CGTTCTTCAA	GGGATACCGG	720
CCGCAGTTCT	ACTTCCGGAC	GACGGACGTG	ACCGGAACGG	TGAAGCTGCC	GGACAACGTG	780
GAGATGGTGA	TGCCGGGAGA	CAACATCGCC	ATCGAGGTGG	AGCTCATTAC	TCCGGTCGCC	840
ATGGAGAAGG	AGCTGCCGTT	CGCCATCCGT	GAGGGTGGCC	GCACGGTGGG	CGCCGGC	897

(2) INFORMATION FOR SEQ ID NO: 167:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 894 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Streptococcus pyogenes
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

AACATGATCA	CTGGTGCCGC	TCAAATGGAC	GGAGCTATCC	TTGTAGTTGC	TTCAACTGAT	60
GGACCAATGC	CACAAACTCG	TGAGCACATC	CTTCTTTCAC	GTCAGGTTGG	TGTTAAACAC	120
CTTATCGTGT	TCATGAACAA	AGTTGACCTT	GTTGATGACG	AAGAGTTGCT	TGAATTAGTT	180
GAGATGGAAA	TTCGTGACCT	TCTTTCAGAA	TACGATTTCC	CAGGTGATGA	CCTTCCAGTT	240
ATCCAAGGTT	CAGCTCTTAA	AGCTCTTGAA	GGCGACACTA	AATTTGAAGA	CATCATCATG	300

- 151 -

GAATTGATGG	ATACTGTTGA	TTCATACATT	CCAGAACCAG	AACGCGACAC	TGACAAACCA	360
TTGCTTCTTC	CAGTCGAAGA	CGTATTCTCA	ATTACAGGTC	GTGGTACAGT	TGCTTCAGGA	420
CGTATCGACC	GTGGTACTGT	TCGTGTCAAC	GACGAAATCG	AAATCGTTGG	TATCAAAGAA	480
GAAACTAAAA	AAGCTGTTGT	TACTGGTGTT	GAAATGTTCC	GTAAACAACT	TGACGAAGGT	540
CTTGCAGGAG	ACAACGTAGG	TATCCTTCTT	CGTGGTGTTC	AACGTGACGA	AATCGAACGT	600
GGTCAAGTTA	TTGCTAAACC	AAGTTCAATC	AACCCACACA	CTAAATTCAA	AGGTGAAGTA	660
TATATCCTTT	CTAAAGACGA	AGGTGGACGT	CACACTCCAT	TCTTCAACAA	CTACCGTCCA	720
CAATTCTACT	TCCGTACAAC	TGACGTAACA	GGTTCAATCG	AACTTCCAGC	AGGTACAGAA	780
ATGGTTATGC	CTGGTGATAA	CGTGACAATC	AACGTTGAGT	TGATCCACCC	AATCGCCGTA	840
GAACAAGGTA	CTACTTTCTC	AATCCGTGAA	GGTGGACGTA	CTGTTGGTTC	AGGT	894

(i) SEQUENCE CHARACTERISTICS:

(2) INFORMATION FOR SEQ ID NO: 168:

- (A) LENGTH: 897 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Thiobacillus cuprinus
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

AACATGATCA	CCGGTGCGGC	CCAGATGGAC	GGCGCCATCC	TGGTCGTGTC	CGCCGCCGAC	60
GGCCCCATGC	CCCAAACCCG	CGAGCACATC	CTGCTGGCGC	GTCAGGTGGG	CGTGCCCTAC	120
ATCATCGTGT	TCCTCAACAA	GTGCGACATG	GTCGACGACG	CCGAGCTGCT	CGAACTCGTC	180
GAGATGGAAG	TGCGCGAGCT	GCTGTCCAAG	TACGACTTCC	CCGGTGACGA	CACCCCCATC	240
ATCAAGGGCT	CGGCCAAGCT	GGCCCTCGAA	GGCGACAAGG	GCGAACTGGG	CGAAGGCGCC	300
ATTCTCAAGC	TGGCCGAGGC	CCTGGACACC	TACATCCCCA	CGCCCGAGCG	GGCCGTCGAC	360
GGCGCGTTCC	TCATGCCCGT	GGAAGACGTG	TTCTCCATCT	CCGGGCGCGG	CACGGTGGTC	420
ACCGGGCGTG	TGGAGCGCGG	CATCATCAAG	GTCGGCGAGG	AAATCGAGAT	TGTCGGCCTC	480
AAGCCCACCC	TCAAGACCAC	CTGCACCGGC	GTGGAAATGT	TCAGGAAGCT	GCTCGACCAG	540
GGCCAGGCCG	GCGACAACGT	CGGCATCTTG	CTGCGCGGCA	CCAAGCGCGA	GGAAGTCGAG	600
CGCGGCCAGG	TGCTGTGCAA	ACCCGGCTCG	ATCAAGCCCC	ACACCCACTT	CACCGCCGAG	660

GTGTACGTGC	TGAGCAAGGA	CGAGGGCGGC	CGCCACACCC	CCTTCTTCAA	CAACTACCGC	720
CCGCAGTTCT	ACTTCCGCAC	CACCGACGTC	ACCGGCGCCA	TCGAACTGCC	CAAGGACAAG	780
GAAATGGTCA	TGCCCGGCGA	TAATGTGAGC	ATCACCGTCA	AGCTCATCGC	CCCCATCGCC	840
ATGGAAGAAG	GCCTGCGCTT	CGCCATCCGC	GAAGGCGGCC	GCACCGTCGG	CGCCGGC	897

- (2) INFORMATION FOR SEQ ID NO: 169:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 894 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Treponema pallidum
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

AATATGATCA C	GGGTGCTGC	GCAGATGGAC	GGTGGTATTC	TCGTCGTGTC	TGCGCCTGAC	60
GGCGTTATGC C	ACAGACGAA	GGAGCATCTT	CTGCTCGCCC	GTCAGGTTGG	TGTTCCCTCC	120
ATCATTGTTT T	TTTGAACAA	GGTTGATTTG	GTTGATGATC	CTGAGTTGCT	AGAGCTGGTG	180
GAAGAAGAGG T	GCGTGATGC	GCTTGCTGGA	TATGGGTTTT	CGCGTGAGAC	GCCTATCGTC	240
AAGGGTCTG C	GTTTAAAGC	TCTGCAGGAT	GGCGCTTCCC	CGGAGGATGC	AGCTTGTATT	300
GAGGAACTGC T	TGCGGCCAT	GGATTCCTAC	TTTGAAGACC	CAGTGCGTGA	CGACGCAAGA	360
CCTTTCTTGC T	CTCTATCGA	GGATGTGTAC	ACTATTTCTG	GGCGTGGTAC	CGTTGTCACG	420
GGGCGCATCG A	ATGTGGGGT	AATTAGTCTG	AATGAAGAGG	TCGAGATCGT	CGGGATTAAG	480
CCCACTAAGA A	AACAGTGGT	TACTGGCATT	GAGATGTTTA	ATAAGTTGCT	TGATCAGGGA	540
ATTGCAGGTG A	TAACGTGGG	GCTGCTTTTG	CGCGGGGTGG	ATAAAAAAGA	GGTTGAGCGC	600
GGTCAGGTGC T	TTCTAAGCC	CGGTTCTATT	AAGCCACACA	CCAAGTTTGA	GGCGCAGATC	660
TACGTGCTCT C	TAAGGAAGA	GGGTGGCCGT	CACAGTCCTT	TTTTTCAAGG	TTATCGTCCG	720
CAGTTTTATT T	TAGAACTAC	TGACATTACC	GGTACGATTT	CTCTTCCTGA	AGGGGTAGAC	780
ATGGTGAAGC C	GGGGGATAA	CACCAAGATT	ATAGGTGAGC	TCATCCACCC	GATAGCTATG	840
GACAAGGGTC T	GAAGCTTGC	GATTCGTGAA	GGGGGGCGCA	CTATTGCTTC	TGGT	894

- (2) INFORMATION FOR SEQ ID NO: 170:
 - (i) SEQUENCE CHARACTERISTICS:

- 153 -

- (A) LENGTH: 891 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Ureaplasma urealyticum
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

AATATGATTA CAGGGGCAGC ACAAATGGAT GGAGCAATTT TAGTTATTGC TGCATCTGAT 60 GGGGTTATGG CTCAAACTAA AGAACATATT TTATTAGCAC GTCAAGTTGG TGTTCCAAAA 120 ATCGTTGTTT TCTTAAACAA ATGTGATTTC ATGACAGATC CAGATATGCA AGATCTTGTT 180 GAAATGGAAG TTCGTGAATT ATTATCTAAA TATGGATTTG ATGGCGATAA CACACCAGTT 240 ATTCGTGGTT CAGGTCTTAA GGCTTTAGAA GGAGATCCAG TTTGAGAAGC AAAAATTGAT 300 GAATTAATGG ACGCAGTTGA TTCATGAATT CCATTACCAG AACGTAGTAC TGACAAACCA 360 TTCTTATTAG CAATTGAAGA TGTATTCACA ATTTCAGGAC GTGGTACAGT AGTAACTGGA 420 CGTGTTGAAC GTGGTGTATT AAAAGTTAAT GATGAGGTTG AAATTGTTGG TCTAAAAGAC 480 ACTCAAAAAA CTGTTGTTAC AGGAATTGAA ATGTTTAGAA AATCATTAGA TCAAGCTGAA 540 GCTGGTGATA ATGCTGGTAT TTTATTACGT GGTATTAAAA AAGAAGATGT TGAACGTGGT 600 CAAGTACTTG TAAAACCAGG ATCAATTAAA CCTCACCGTA CTTTTACTGC TAAAGTTTAT 660 ATTCTTAAAA AAGAAGAAGG TGGACGTCAT ACACCTATTG TTTCAGGATA CCGTCCACAA 720 TTCTATTTTA GAACAACAGA TGTAACAGGT GCTATTTCAT TACCTGCTGG TGTTGATTTG 780 GTTATGCCAG GTGATGACGT TGAAATGACT GTAGAATTAA TTGCTCCAGT TGCGATTGAA 840 GATGGATCTA AATTCTCAAT CCGTGAAGGT GGTAAAACTG TAGGTCATGG T 891

- (2) INFORMATION FOR SEQ ID NO: 171:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 909 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Wolinella succinogenes
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

AACATGATTA	CAGGTGCTGC	TCAAATGGAT	GGCGCGATTC	TTGTTGTTTC	TGCGGCGGAT	60
GGCCCCATGC	CCCAAACTAG	GGAGCACATT	CTTCTTTCTC	GACAAGTAGG	CGTTCCTTAC	120
ATCGTGGTTT	TCTTGAACAA	AGAAGATATG	GTTGATGACG	CTGAGCTTCT	TGAGCTTGTT	180
GAAATGGAAG	TTAGAGAACT	TCTTAGCAAC	TACGACTTCC	CTGGAGATGA	CACTCCTATC	240
GTTGCAGGTT	CCGCTCTTAA	AGCTCTTGAA	GAGGCTAACG	ACCAGGAAAA	TGTTGGCGAG	300
TGGGGCGAGA	AAGTATTGAA	GCTTATGGCT	GAGGTTGACC	GATATATTCC	TACGCCTGAG	360
CGAGATGTGG	ATAAGCCTTT	CCTTATGCCT	GTTGAAGACG	TATTCTCCAT	CGCGGGTCGT	420
GGAACCGTTG	TGACAGGAAG	AATTGAAAGA	GGCGTGGTTA	AAGTCGGTGA	CGAAGTAGAA	480
ATCGTTGGTA	TCCGAAACAC	ACAAAAAACA	ACCGTAACTG	GCGTTGAGAT	GTTCCGAAAA	540
GAGCTCGACA	AGGGTGAGGC	GGGTGACAAC	GTTGGTGTTC	TTTTGAGAGG	CACCAAGAAA	600
GAAGATGTTG	AGAGAGGTAT	GGTTCTTTGT	AAAATAGGTT	CTATCACTCC	TCACACTAAC	660
FTTGAAGGTG	AAGTTTACGT	TCTTTCCAAA	GAGGAAGGCG	GACGACACAC	TCCATTCTTC	720
AATGGATACC	GACCTCAGTT	CTATGTTAGA	ACTACAGACG	TTACCGGTTC	TATCTCTCTT	780
CCTGAGGGCG	TAGAGATGGT	TATGCCTGGT	GACAACGTTA	AGATCAATGT	TGAGCTTATC	840
GCTCCTGTAG	CCCTCGAAGA	GGGAACACGA	TTCGCGATCC	GTGAAGGTGG	TCGAACCGTT	900
GGTGCGGGT						909

(2) INFORMATION FOR SEQ ID NO: 172:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:6
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:12
 - (D) OTHER INFORMATION:/note= "n = inosine"
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:18
 - (D) OTHER INFORMATION:/note= "n = inosine"

- 155 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:	
TARTCNGTRA ANGCYTCNAC RCACAT	26
(2) INFORMATION FOR SEQ ID NO: 173:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:	
TCTTTAGCAG AACAGGATGA A	21
(2) INFORMATION FOR SEQ ID NO: 174:	
 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 	
(ii) MOLECULE TYPE: DNA (genomic)	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:	
GAATAATTCC ATATCCTCCG	20

20

CLAIMS

What is claimed is:

- 1. A method using probes and/or amplification primers which are specific, ubiquitous and sensitive for determining the presence and/or amount of nucleic acids:
- from a bacterial antibiotic resistance gene selected from the group consisting of bla_{tem} , bla_{shv} , bla_{rob} , bla_{oxa} , blaZ, aadB, aacC1, aacC2, aacC3, aacG'-lla, aacA4, aad(6'), vanA, vanB, vanC, msrA, satA, aac(6')-aph(2''), vat, vga, ermA, ermB, ermC, mecA, int and sul, and
- from specific bacterial and fungal species selected from the group consisting of Enterococcus faecium, Listeria monocytogenes, Neisseria meningitidis, Staphylococcus saprophyticus, Streptococcus agalactiae, Candida albicans, Enterococcus species, Neisseria species, Staphylococcus species, Streptococcus species and Candida species,

in any sample suspected of containing said bacterial and/or fungal nucleic acids,

wherein each of said nucleic acid or variant or part thereof comprises a selected target region hybridizable with said probes or primers;

said method comprising the following steps: contacting said sample with said probes or primers and detecting the presence and/or amount of hybridized probes or amplified products as an indication of the presence and/or amount of said specific bacterial and/or fungal species and bacterial antibiotic resistance genes.

- 2. A method according to claim 1, which further makes use of probes and/or primers which are specific, ubiquitous and sensitive for determining the presence and/or amount of nucleic acids from any bacterium or fungus.
- 3. The method of claim 1, which is performed directly from a test sample.
- 25 4. The method of claim 1, which is performed directly from a test sample consisting of a bacterial and/or fungal culture or suspension.
 - 5. The method of claim 1, wherein said nucleic acids are all detected under uniform hybridization or amplification conditions.
- 6. The method of claim 1, wherein said nucleic acids are amplified by a method selected from the group consisting of:
 - a) polymerase chain reaction (PCR),
 - b) ligase chain reaction (LCR),
 - c) nucleic acid sequence-based amplification (NASBA),

SUBSTITUTE SHEET (RULE 26)

10

15

20

25

30

- d) self-sustained sequence replication (3SR),
- e) strand displacement amplification (SDA),
- f) branched DNA signal amplification (bDNA),
- g) transcription-mediated amplification (TMA),
- h) cycling probe technology (CPT),
- i) nested PCR, and
- j) multiplex PCR.
- 7. The method of claim 6, wherein said nucleic acids are amplified by PCR.
- 8. The method of claim 7, wherein the PCR protocol achieves within one hour under uniform amplification conditions the determination of the presence of said nucleic acids by performing for each amplification cycle an annealing step of thirty seconds at 45-55°C and a denaturation step of only one second at 95°C without any time specifically allowed to an elongation step.
- 9. A method for the detection, identification and/or quantification of a microorganism selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, directly from a test sample or from bacterial and/or fungal cultures, which comprises the following steps:
 - a) depositing and fixing on an inert support or leaving in solution the said microorganism DNA of the sample or of a substantially homogeneous population of said microorganism isolated from this sample, or
 - inoculating said sample or said substantially homogeneous population of microorganism isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or said isolated microorganism to release the said microorganism DNA,

said microorganism DNA being made in a substantially single-stranded form;

b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleic acid which nucleotide sequence is selected from the group consisting of SEQ ID NOs: 26, 27, 28, 29, 30, 120, 131 to 134, 31, 140 to 143, 32 to 36, 120 to 124, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of *Enterococcus faecium*, *Listeria*

10

15

20

25

30

35

monocytogenes, Neisseria meningitidis, Staphylococcus saprophyticus, Streptococcus agalactiae, Candida albicans, Enterococcus species, Neisseria species, Staphylococcus species, Streptococcus species and Candida species, respectively, under conditions such that the nucleic acid of said probe can selectively hybridize with said microorganism DNA, whereby a hybridization complex is formed; and

- c) detecting the presence of said hybridization complex on said inert support or in said solution as an indication of the presence and/or amount of said microorganism, in said test sample.
- 10. A method for detecting the presence and/or amount of a microorganism selected from the group consisting of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species, *Streptococcus* species and *Candida* species, in a test sample which comprises the following steps:
- a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said microorganism DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 26, 27, 28, 29, 30, 120, 131 to 134, 31, 140 to 143, 32 to 36, 120 to 124, respectively with regard to said microorganism, a sequence complementary thereof, and a variant thereof;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
 - c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of said microorganisms, in said test sample.
 - 11. The method of claim 10, wherein said pair of primers is defined in SEQ ID NOs: 1 and 2, 3 and 4, 5 and 6, 7 and 8, 9 and 10, 11 and 12, 13 and 14, 15 and 16, 17 to 20, 21 and 22, respectively, for each of *Enterococcus faecium*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Candida albicans*, *Enterococcus* species, *Neisseria* species, *Staphylococcus* species and *Streptococcus* species.

20

25

30

35

- 12. A method for detecting the presence and/or amount of any bacterium directly from a test sample or a bacterial culture, which comprises the following steps:
- a) depositing and fixing on an inert support or leaving in solution the bacterial DNA of the sample or of a substantially homogeneous population of bacteria isolated from this sample, or

inoculating said sample or said substantially homogeneous population of bacteria isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated bacteria to release the bacterial DNA,

said bacterial DNA being made in a substantially single-stranded form;

- b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleic acid which nucleotide sequence is selected from the group consisting of SEQ ID NOs: 118, 119, 125 to 171, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of any bacterial species, under conditions such that the nucleic acid of said probe can selectively hybridize with said bacterial DNA, whereby a hybridization complex is formed; and
 - c) detecting the presence of said hybridization complex on said inert support or in said solution as an indication of the presence and/or amount of any bacterium in said test sample.
 - 13. A method for detecting the presence and/or amount of any bacterium in a test sample which comprises the following steps:
 - a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of any bacterial DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NO: 118, 119, 125 to 171, a sequence complementary thereof, and a variant thereof;
 - b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
 - c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of any bacterium in said test sample.

10

15

20

25

30

35

- 14. The method of claim 13, wherein said pair of primers is defined in SEQ ID NOs: 23 and 24.
- 15. A method for obtaining *tuf* sequences from any bacterium directly from a test sample or a bacterial culture, which comprises the following steps:
- a) treating said sample with an aqueous solution containing a pair of primers having a sequence selected within the nucleotide sequences defined in SEQ ID NOs: 107 and 108, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, and a variant thereof, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said bacterial *tuf* gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
 - c) detecting the presence and/or amount of said amplified target sequence; and
- d) determining the nucleotide sequence of the said amplified target sequence by using any DNA sequencing method.
- 16. A method for detecting the presence and/or amount of any fungus directly from a test sample or a fungal culture, which comprises the following steps:
 - a) depositing and fixing on an inert support or leaving in solution the fungal DNA of the sample or of a substantially homogeneous population of fungi isolated from this sample, or

inoculating said sample or said substantially homogeneous population of fungi isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated fungi to release the fungal DNA,

said fungal DNA being made in a substantially single-stranded form;

- b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleotide sequence selected from the group consisting of SEQ ID NOs: 120 to 124, a sequence complementary thereof, a part thereof having at least 12 nucleotides in length, and a variant thereof, which specifically and ubiquitously anneals with strains or representatives of any fungus, under conditions such that the nucleic acid of said probe can selectively hybridize with said fungal DNA, whereby a hybridization complex is formed; and
 - c) detecting the presence of said hybridization complex on said inert support or SUBSTITUTE SHEET (RULE 26)

10

15

20

25

30

35

in said solution as an indication of the presence and/or amount of any fungus in said test sample.

- 17. A method for detecting the presence and/or amount of any fungus in a test sample which comprises the following steps:
- a) treating said sample with an aqueous solution containing at least one pair of oligonucleotide primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of any fungal DNA that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 120 to 124, a sequence complementary thereof, and a variant thereof;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
- c) detecting the presence and/or amount of said amplified target sequence as an indication of the presence and/or amount of any fungus in said test sample.
- 18. A method for obtaining *tuf* sequences from any fungus directly from a test sample or a fungal culture, which comprises the following steps:
- a) treating said sample with an aqueous solution containing a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 109 and 172, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, and a variant thereof, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said fungal *tuf* gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
 - c) detecting the presence and/or amount of said amplified target sequence; and
- d) determining the nucleotide sequence of the said amplified target sequence by using any DNA sequencing method.
- 19. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance mediated by a bacterial antibiotic resistance gene selected

from the group consisting of bla_{oxa} , blaZ, aac6'-lla, ermA, ermB, ermC, vanB, vanC, directly from a test sample or a bacterial culture, which comprises the following steps:

a) depositing and fixing on an inert support or leaving in solution the bacterial DNA of the sample or of a substantially homogeneous population of bacteria isolated from this sample, or

inoculating said sample or said substantially homogeneous population of bacteria isolated from this sample on an inert support, and lysing *in situ* said inoculated sample or isolated bacteria to release the bacterial DNA,

said bacterial DNA being made in a substantially single-stranded form;

10

5

- b) contacting said single-stranded DNA with a probe, said probe comprising at least one single-stranded nucleotide sequence having at least 12 nucleotide in length is selected from the group consisting of SEQ ID NOs: 110, 111, 112, 113, 114 115, 116, 117, a sequence complementary thereof, and a variant thereof, which specifically hybridizes with said bacterial antibiotic resistance gene, respectively; and
- 15

20

25

30

35

- c) detecting the presence of a hybridization complex as an indication of a bacterial resistance mediated by said one of said bacterial antibiotic resistance genes.
- 20. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance mediated by a bacterial antibiotic resistance gene selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-lla*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*, directly from a test sample or a bacterial culture, which comprises the following steps:
- a) treating said sample with an aqueous solution containing at least one pair of primers having at least 12 nucleotides in length, one of said primers being capable of hybridizing selectively with one of the two complementary strands of said bacterial antibiotic resistance gene that contains a target sequence, and the other of said primers being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template, said at least one pair of primers being chosen from a nucleotide sequence within the group consisting of SEQ ID NOs: 110, 111, 112, 113, 114, 115, 116, 117, respectively with regard to said bacterial antibiotic resistance gene, a sequence complementary thereof, and a variant thereof;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
- c) detecting the presence and/or amount of said amplified target sequence as an indication of a bacterial resistance mediated by one of said bacterial antibiotic resistance genes.

 SUBSTITUTE SHEET (RULE 26)

10

15

20

25

30

- 21. A method as defined in claim 1, which comprises the evaluation of the presence of a bacterial resistance gene selected from the group consisting of bla_{tem} , bla_{shv} , bla_{rob} , bla_{oxa} , bla_{Oxa
- a) treating said sample with an aqueous solution containing at least one pair of primers having a sequence selected in the group consisting of SEQ ID NOs: 37 to 40, 41 to 44, 45 to 48, 49 and 50, 51 and 52, 53 and 54, 55 and 56, 57 and 58, 59 to 60, 61 to 64, 65 and 66, 173 and 174, 67 to 70, 71 to 74, 75 and 76, 77 to 80, 81 and 82, 83 to 86, 87 and 88, 89 and 90, 91 and 92, 93 and 94, 95 and 96, 97 and 98, 99 to 102, 103 to 106, a part thereof having at least 12 nucleotides in length, a sequence complementary thereof, a variant thereof, and mixtures thereof, one of said primers of said pair being capable of hybridizing selectively with one of the two complementary strands of its respective bacterial antibiotic resistance gene that contains a target sequence, and the other of said primers of said pairs being capable of hybridizing with the other of said strands so as to form an extension product which contains the target sequence as a template;
- b) synthesizing an extension product of each of said primers, said extension product containing the target sequence, and amplifying said target sequence, if any, to a detectable level; and
- c) detecting the presence and/or amount of said amplified target sequence as an indication of a bacterial resistance mediated by one of said bacterial antibiotic resistance genes.
- 22. A nucleic acid having the nucleotide sequence of any one of SEQ ID NOs: 26 to 36, 110 to 171, a part thereof, a sequence complementary thereof, and variant thereof which, when in single-stranded form, ubiquitously and specifically hybridizes with a target bacterial or fungal DNA as a probe or as a primer.
- 23. An oligonucleotide having the nucleotide sequence of any one of SEQ ID NOs: 1 to 25, 37 to 109, 172 to 174, a part thereof, a sequence complementary thereof, and variant thereof, which ubiquitously and specifically hybridizes with a target bacterial or fungal DNA as a probe or as a primer.
- 24. A recombinant plasmid comprising a nucleic acid as defined in claim 22.
- 25. A recombinant host which has been transformed by a recombinant plasmid according to claim 24.
- 35 26. A recombinant host according to claim 25 wherein said host is Escherichia coli.
 - 27. A diagnostic kit for the detection and/or quantification of the nucleic acids of any SUBSTITUTE SHEET (RULE 26)

20

25

30

35

combination of the microbial species and/or genera selected from the group consisting of Enterococcus faecium, Listeria monocytogenes, Neisseria meningitidis, Staphylococcus saprophyticus, Streptococcus agalactiae, Candida albicans, Enterococcus species, Neisseria species, Staphylococcus species, Streptococcus species and Candida species, comprising any suitable combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 26 to 36, 120 to 124, 131 to 134, 140 to 143, sequences complementary thereof, and variants thereof.

- 28. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the microbial species and/or genera selected from the group consisting of Enterococcus faecium, Listeria monocytogenes, Neisseria meningitidis, Staphylococcus saprophyticus, Streptococcus agalactiae, Candida albicans, Enterococcus species, Neisseria species, Staphylococcus species, Streptococcus species and Candida species, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 26 to 36, 120 to 124, 131 to 134, 140 to 143, sequences complementary thereof, and variants thereof.
 - 29. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the microbial species and/or genera selected from the group consisting of Enterococcus faecium, Listeria monocytogenes, Neisseria meningitidis, Staphylococcus saprophyticus, Streptococcus agalactiae, Candida albicans, Enterococcus species, Neisseria species, Staphylococcus species and Streptococcus species, comprising any suitable combination of primers selected from the group consisting of SEQ ID NOs: 1 to 22, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.
 - 30. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of bla_{oxa}, blaZ, aac6'-lla, ermA, ermB, ermC, vanB, vanC, comprising any suitable combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof.
 - 31. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of bla_{oxa}, blaZ, aac6'-lla, ermA, ermB, ermC, vanB, vanC, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof.

10

15

32. A diagnostic kit for the detection and/or quantification of the nucleic acids of any combination of the bacterial resistance genes selected from the group consisting of bla_{tem} , bla_{shv} , bla_{rob} , bla_{oxa} ,

A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium and/or fungus, comprising any combination of probes of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof.

- 34. A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium and/or fungus, comprising any suitable combination of primers of at least 12 nucleotides in length selected from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof.
- 35. A diagnostic kit for the detection and/or quantification of the nucleic acids of any bacterium, comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof.
- 20 36. A diagnostic kit, as defined in claim 27, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.
- 37. A diagnostic kit, as defined in claim 28, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.
- 38. A diagnostic kit, as defined in claim 29, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.
- 35 39. A diagnostic kit, as defined in claim 27, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from

20

the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of bla_{oxa} , blaZ, aac6'-lla, ermA, ermB, ermC, vanB, vanC.

- 5 40. A diagnostic kit, as defined in claim 28, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 110 to 117, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of *bla_{oxa}*, *blaZ*, *aac6'-lla*, *ermA*, *ermB*, *ermC*, *vanB*, *vanC*.
 - 41. A diagnostic kit, as defined in claim 29, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 37 to 106, 173 and 174, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterial antibiotic resistance gene selected from the group consisting of bla_{tem}, bla_{rob} bla_{shv} bla_{oxa} blaZ, aadB, aacC1, aacC2, aacC3, aacA4, aac6'-Ila, aad(6'), ermA, ermB, ermC, mecA, vanA, vanB, vanC, satA, aac(6')-aph(2"), vat, vga, msrA, sul and int.
 - 42. A diagnostic kit, as defined in claim 30, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.
- 43. A diagnostic kit, as defined in claim 31, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.
- 44. A diagnostic kit, as defined in claim 32, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.
- 45. A diagnostic kit, as defined in claim 39, further comprising any combination of probes of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic

acids of any bacterium and/or fungus.

- 46. A diagnostic kit, as defined in claim 40, further comprising any suitable combination of primers of at least 12 nucleotides in length selected within a nucleotide sequence from the group consisting of SEQ ID NOs: 118 to 171, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium and/or fungus.
- 47. A diagnostic kit, as defined in claim 41, further comprising a pair of primers having a sequence selected within the nucleotide sequence defined in SEQ ID NOs: 23 and 24, parts thereof having at least 12 nucleotides in length, sequences complementary thereof, and variants thereof, for the simultaneous detection and/or quantification of nucleic acids of any bacterium.

Inter. onal Application No PCT/CA 97/00829

, .	· · · · · · · · · · · · · · · · · · ·	10.70.	
A. CLASSI IPC 6	ification of subject matter C12Q1/68		2 .
	o International Patent Classifloation (IPC) or to both national classif	ication and IPC	
	SEARCHED	·	
IPC 6	coumentation searched (classification system followed by classification classification system followed by cl	ation symbols)	
Documenta	tion searched other than minimum documentation to the extent tha	such documents are included in the field	is searched . ·., -
Electronic d	lata base consulted during the international search (name of data l	oase and, where practical, search terms t	ised)
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category ^o	Citation of document, with indication, where appropriate, of the r	elevant passages	Relevant to claim No.
Х	WO 96 08582 A (BERGERON MICHEL G; OUELLETTE MARC (CA); ROY PAUL H (CA)) 21 March 1996 see whole document, esp claims 1-3		1-14, 19-38, 40-47
X	FR 2 699 539 A (PASTEUR INSTITUT) 24 June 1994 see whole document, esp. abstract and claims		1-8,19, 32
		-/	
X Furti	her documents are listed in the continuation of box C.	Patent family members are lis	ted in annex.
"A" docume consid "E" earlier of filing d "L" docume which citation "O" docume other r "P" docume later th	ont which may throw doubts on priority claim(s) or is oited to establish the publication date of another n or other special reason (as specified) ent referring to an oral disolosure, use, exhibition or	T later document published after the or priority date and not in conflicticited to understand the principle of invention "X" document of particular relevance; to cannot be considered novel or oal involve an inventive step when the "Y" document of particular relevance; to cannot be considered to involve a document is combined with one of membs, such combination being of in the art. "&" document member of the same patents of mailing of the international of the same patents.	with the application but or theory underlying the he claimed invention nnot be considered to e document is taken alone he claimed invention n inventive step when the r more other such docuvoious to a person skilled ent family search report
8	June 1998	0 1. 07. 98	
Name and n	nailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Eav. (431-70) 340-2016	Authorized officer Müller, F	

3

Interr. Just Application No PCT/CA 97/00829

Relevant to claim No. 13,31, 33,36, 37,42, 43,45,46
33,36, 37,42, 43,45,46
1,19,20, 22,30, 31,39,40
1,19,20, 22,30, 31,39,40

Inten anal Application No
PCT/CA 97/00829

ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
LOECHEL S. ET AL.,: "Nucleotide sequence of the tuf gene from Mycoplasma genitalium" NUCLEIC ACID RESEARCH, vol. 17, no. 23, - 1989 page 10127 XP002066858 see the whole document & DATABASE EMPRO EMBL AC:X16463	12,13, 33,34, 36,37, 42,43,45	
WO 96 18745 A (SMITHKLINE BEECHAM CORP; HOYER LOIS L (US); LIVI GEORGE P (US); SH) 20 June 1996	1-12,16, 17, 22-29, 33,34, 36,37, 42,43, 45,46	
see the whole document & DATABASE GENESEQ DERWENT AC:T29069,		
US 5 523 205 A (COSSART PASCALE ET AL) 4 June 1996 see the whole document	1-9	
EP 0 761 815 A (SANDOZ AG ;SANDOZ LTD (CH); SANDOZ AG (DE)) 12 March 1997 see the whole document & DATABASE GENESEQ DERWENT AC:T87876	1,21	
PORCELLA S. ET AL.,: "Identification of an EF-Tu protein that is priplasm-associated and processed in Neisseria gonorrhoeae" MICROBIOLOGY, vol. 142, - September 1996 pages 2481-2489, XP002066859 see the whole document & DATABASE EMPRO EMBL AC:L36380	1-8,12, 13,22, 33,34, 36,37, 42,43, 45,46	
	LOECHEL S. ET AL.,: "Nucleotide sequence of the tuf gene from Mycoplasma genitalium" NUCLEIC ACID RESEARCH, vol. 17, no. 23, - 1989 page 10127 XP002066858 see the whole document & DATABASE EMPRO EMBL AC:X16463 WO 96 18745 A (SMITHKLINE BEECHAM CORP; HOYER LOIS L (US); LIVI GEORGE P (US); SH) 20 June 1996 see the whole document & DATABASE GENESEQ DERWENT AC:T29069, US 5 523 205 A (COSSART PASCALE ET AL) 4 June 1996 see the whole document EP 0 761 815 A (SANDOZ AG; SANDOZ LTD (CH); SANDOZ AG (DE)) 12 March 1997 see the whole document & DATABASE GENESEQ DERWENT AC:T87876 PORCELLA S. ET AL.,: "Identification of an EF-Tu protein that is priplasm-associated and processed in Neisseria gonorrhoeae" MICROBIOLOGY, vol. 142, - September 1996 pages 2481-2489, XP002066859 see the whole document & DATABASE EMPRO EMBL	

3

Intern risi Application No
PCT/CA 97/00829

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT			//00829	
C.(Continua Category °	tition) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.	
			newant to claim No.	
X	BREMAUD L. ET AL.,: "genetic and molecular analysis of the tRNA-tufB operon of the mycobactreium Stigmatella aurantiaca" NUCLEIC ACID RESEARCH, vol. 23, no. 10, - 1995 pages 1737-1743, XP002067242 see the whole document & DATABASE EMPRO EMBL AC:X82820		22,33	
X	DATABASE EMPRO EMBL 2 July 1986 MURPHY E. ET AL.,: XP002067252 AC:X03216		22	
X	EAST A.K. & DYKE K.G.H.: "Cloning and sequence dtermination of six staphylococcus aureus b-lactamases and their expression in E. coli and S. aureus" J. GEN. MICROBIOL., vol. 135, - 4 April 1989 pages 1001-1015, XP002067243 see the whole document & DATABASE EMPRO EMBL AC:M25253		22	
x	BRISSON-NOEL A. ET AL.,: "Evidence for natural gene transfer from gram-positive cocci to E. coli" J. BACTERIOL, vol. 170, - April 1988 pages 1739-1745, XP002067244 see the whole document & DATABASE EMPRO EMBL AC:M19270		22	
x	AN G. & FRIESEN J.D.: "The nucleotide sequence of tufB and four nearby tRNA structural genes of E. coli" GENE, vol. 12, - December 1980 pages 33-39, XP002067245 see the whole document & DATABASE EMPRO EMBL AC:X57091		22	
	-/			

Inter Snal Application No PCT/CA 97/00829

C (Continue	PCT/CA 9//00829			
C.(Continua Category °	C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.			
	una incomentante deprepriese, un una rerovent passages	Helevant to claim No.		
X	OHAMA T. ET AL.,: "Organization and codon usage of the streptomycin operon in micrococcus luteus, a bacterium with a high genomic G+C content" J. BACTERIOL., vol. 169, - October 1987 pages 4770-4777, XP002067246 see the whole document & DATABASE EMPRO EMBL AC:M17788	22		
X	MONOD M. ET AL.,: "Sequence and properties of pIM13, a macrolide-lincosamide-steptogramin B resistance plasmid from bacillus subtilis" J. BACTERIOL., vol. 167, - July 1986 pages 138-147, XP002067247 see the whole document & DATABASE EMPRO embl AC:X63539	22		
X	CARLIN N. ET AL.,: "Monoclonal antibodies specific for elongation factor Tu and complete nucleotide sequence of the tuf gene in M. tuberculosis" INFECT. IMMUN., vol. 60, August 1992, pages 3136-3142, XP002067248 see the whole document & DATABASE EMPRO EMBL AC:X63539	22		
X	ZHANG Y-X. ET AL.,: "Cloning, sequencing, and expression in E. coli of the gene encoding a 45-kilodalton protein, elongation factor Tu, from chlamydia trachomatis serovar F" J. BACTERIOL, vol. 176, no. 4, - February 1994 pages 1184-1187, XP002067249 see the whole document & DATABASE EMPRO EMBL AC:L22216	22		
x	DATABASE EMPRO emb1 13 August 1995 PERLEE L. & SCHWARTZ I.: XP002067253 AC:L23125	22		
	-/			

Inter onal Application No PCT/CA 97/00829

C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PC1/CA 9//00829
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	DATABASE EMPRO EMBL 27 October 1996 YOSHIKAWA H.: XP002067254 AC:D64127	22
X	DATABASE EMPRO EMBL thesis, 8 June 1994 KAMLA V.: XP002067255 AC:Z34275	22
X	ANDERSSON S.G.E.: "Unusual organization of the rRNA genes in Rickettsia prowazekii" J. BACTERIOL., vol. 177, no. 4, - July 1995 pages 4171-4175, XP002067250 see the whole document & DATABASE EMPRO EMBL AC:z54170 see abstract	22
x	SHAW K.J. ET AL.,: "Isolation, characterization and DNA sequence analysis of an AAC(6')_II gene from Pseudomonas aeruginosa" ANTIMICROBIAL. AGNETS AND CHEMOTHERAPY, vol. 33, no. 12, - December 1989 pages 2052-2062, XP002067251 see the whole document & DATABASE EMPRO EMBL AC:X55116	
x	DATABASE EMPRO EMBL LUDWIG W. ET AL.,: "Phylogenetic relationships of bacteria based on comparative sequence analysis of elongation factor Tu and ATP-synthase-beta subunit genes; Antonie van leeuwenhoek 64; 285-305 (1993)" XP002067256 AC: X76863, X76866, X76867, X76871, X76872	22
P,X	EP 0 786 519 A (HUMAN GENOME SCIENCES INC) 30 July 1997 seq id 4	22

PCT/CA 97/00829

BoxI	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	mational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
BoxII	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	emational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1. X	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remar	K on Protest The additional search fees were accompanied by the applicant's protest. X No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-13,19,21-29,32-34,36,41-43,45,46 (partly)

Nucleic acids (SEQ. ID.:1,2,13,14,67-70,51,52, 71-76, 81-86,131-134, 173,174) specific for Enterococcus spp., methods using them, and plasmids, hosts and kits containing them

2. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ ID.: 3,4, 136-139) specific for Listeria monocytogenes, methods using them, and plasmids, hosts and kits containing them

3. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ. ID.: 5,6,15,16,162) specific for Neisseria spp., methods using them, and plasmids, hosts and kits containing them

4. Claims: 1-9,11-13,21-26,32-34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ ID.: 7,8,17-20,77-80,89-98, 140-143) specific for Staphylococcus spp., methods using them, and plasmids, hosts and kits containing them

5. Claims: 1-9,11-13,22-26,29,33,34,36,37,42,43,45,46 (partly)

Nucleic acids (SEQ. ID.: 9,10,21,22,144-146,167) specific for Streptococcus spp., methods using them, and plasmids, hosts and kits containing them

6. Claims: 1-12,22-29,33,34,36,37,42,43,45,46 (partly), 16, 17 (complete)

Nucleic acids (SEQ ID.: 11,12,120-124) specific for Candida albicans, methods using them, and plasmids, hosts and kits containing them

7. Claims: 14,19,20,30,31,35,38,39,40,44,47 (complete), 23, 32 (partly)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Nucleic acids (SEQ ID.: 23-24, 99-106, 110-117, 118,119, 125-130, 135, 147-161, 163-166, 168-171) specific for universal detection of bacteria and fungus species, methods using them, and plasmids, hosts and kits containing them

8. Claims: 15,18 (complete)

Methods for obtaining tuf sequences by using SEQ ID.: 107,108,109 and 172

page 2 of 2

Information on patent family members

Inter anal Application No PCT/CA 97/00829

	·		J1 000E3
Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9608582 A	21-03-1996	AU 3468195 A CA 2199144 A EP 0804616 A NO 971111 A	29-03-1996 21-03-1996 05-11-1997 09-05-1997
FR 2699539 A	24-06-1994	CA 2152066 A EP 0672147 A WO 9414961 A FR 2699537 A JP 8505050 T	07-07-1994 20-09-1995 07-07-1994 24-06-1994 04-06-1996
WO 9618745 A	20-06-1996	US 5668263 A AU 4468696 A CA 2207816 A EP 0820523 A	16-09-1997 03-07-1996 20-06-1996 28-01-1998
US 5523205 A	04-06-1996	AT 121460 T DE 68922252 D DE 68922252 T WO 8906699 A EP 0355147 A JP 2502880 T US 5389513 A	15-05-1995 24-05-1995 24-08-1995 27-07-1989 28-02-1990 13-09-1990 14-02-1995
EP 0761815 A	12-03-1997	AU 6429796 A CA 2184301 A JP 9182590 A	06-03-1997 01-03-1997 15-07-1997
EP 0786519 A	30-07-1997	CA 2194411 A JP 9322781 A	06-07-1997 16-12-1997